Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 05	CASREACT(R) - Over 10 million reactions available
NEWS 4	DEC 14	2006 MeSH terms loaded in MEDLINE/LMEDLINE
NEWS 5	DEC 14	2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
NEWS 6	DEC 14	CA/CAplus to be enhanced with updated IPC codes
NEWS 7	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 8	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 9	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 11	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 12	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 13	JAN 30	Saved answer limit increased
NEWS 14	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 15	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 16	FEB 22	Status of current WO (PCT) information on STN
NEWS 17	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 18	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 19	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 20	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 21	FEB 28	TOXCENTER reloaded with enhancements
NEWS 22	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 23	MAR 01	INSPEC reloaded and enhanced
NEWS 24	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:35:32 ON 07 MAR 2006

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:35:54 ON 07 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAR 2006 HIGHEST RN 876011-49-3
DICTIONARY FILE UPDATES: 6 MAR 2006 HIGHEST RN 876011-49-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

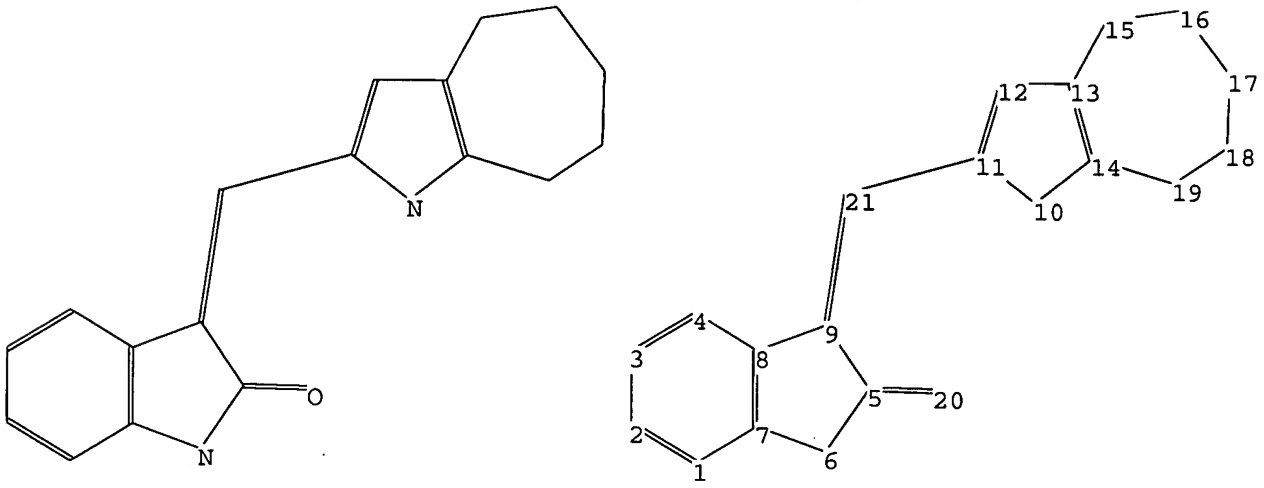
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10733803.str



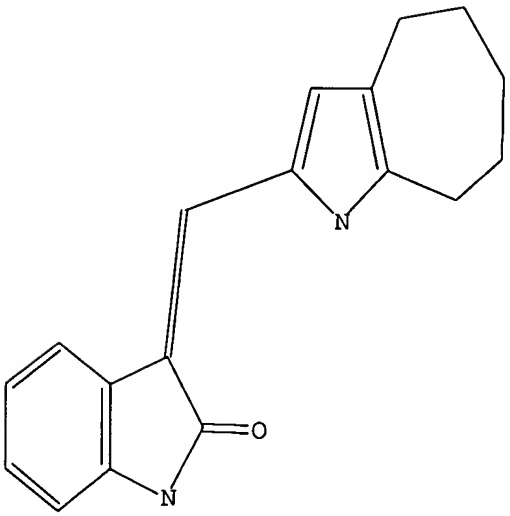
chain nodes :
20 21
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
chain bonds :
5-20 9-21 11-21
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14 13-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
5-6 5-20 6-7 10-11 10-14 11-12 12-13 13-14 13-15 14-19 15-16 16-17 17-18 18-19
exact bonds :
5-9 8-9 9-21 11-21
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8
isolated ring systems :
containing 1 : 10 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:36:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 14:36:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 103 TO ITERATE

100.0% PROCESSED 103 ITERATIONS 76 ANSWERS
SEARCH TIME: 00.00.02

L3 76 SEA SSS FUL L1

=> FIL HCAPLUS
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

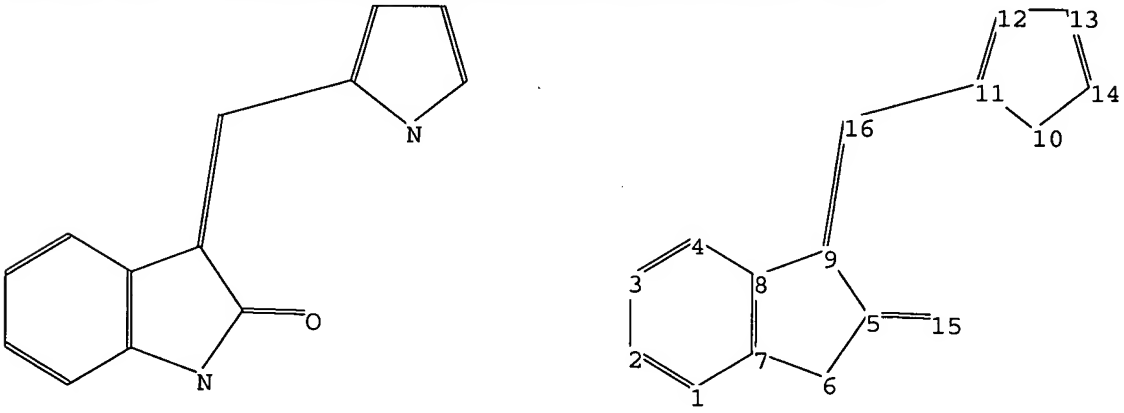
FILE 'HCAPLUS' ENTERED AT 14:36:41 ON 07 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 7 Mar 2006 VOL 144 ISS 11
FILE LAST UPDATED: 6 Mar 2006 (20060306/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 1 L3
=>
Uploading C:\Program Files\Stnexp\Queries\10733803a.str



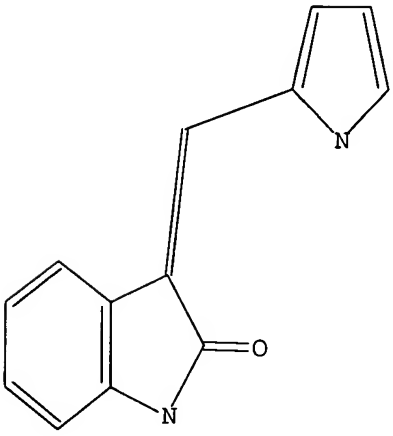
chain nodes :
15 16
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
5-15 9-16 11-16
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :
5-6 5-15 6-7 10-11 10-14
exact bonds :
5-9 8-9 9-16 11-12 11-16 12-13 13-14
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8
isolated ring systems :
containing 1 : 10 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS

L5 STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l5
REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 14:38:08 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 223 TO ITERATE

100.0% PROCESSED 223 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 3565 TO 5355
PROJECTED ANSWERS: 1778 TO 3102

L6 50 SEA SSS SAM L5

L7 26 L6

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.53	175.18

FILE 'REGISTRY' ENTERED AT 14:38:18 ON 07 MAR 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAR 2006 HIGHEST RN 876011-49-3
DICTIONARY FILE UPDATES: 6 MAR 2006 HIGHEST RN 876011-49-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d his

(FILE 'HOME' ENTERED AT 14:35:32 ON 07 MAR 2006)

FILE 'REGISTRY' ENTERED AT 14:35:54 ON 07 MAR 2006
L1 STRUCTURE UPLOADED
L2 3 S L1
L3 76 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 14:36:41 ON 07 MAR 2006
L4 1 S L3
L5 STRUCTURE UPLOADED
S L5

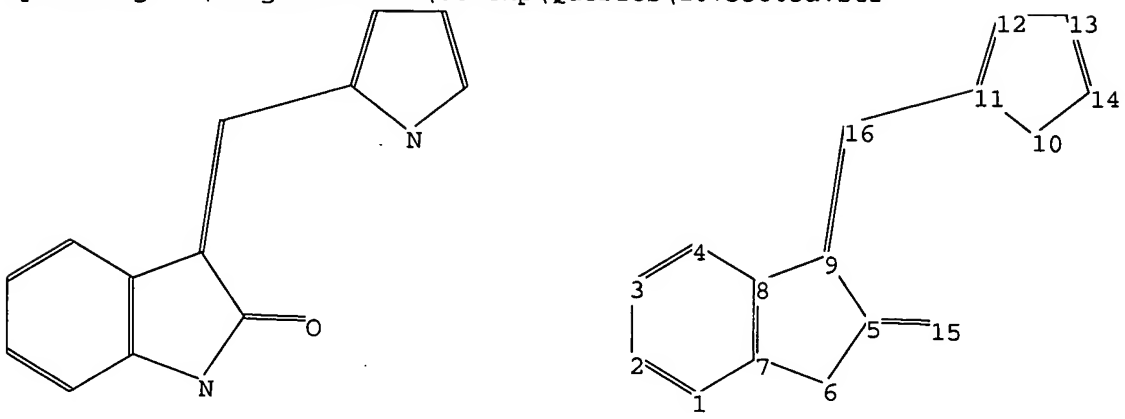
FILE 'REGISTRY' ENTERED AT 14:38:08 ON 07 MAR 2006

L6 50 S L5

FILE 'HCAPLUS' ENTERED AT 14:38:09 ON 07 MAR 2006
L7 26 S L6

FILE 'REGISTRY' ENTERED AT 14:38:18 ON 07 MAR 2006

=>
Uploading C:\Program Files\Stnexp\Queries\10733803a.str



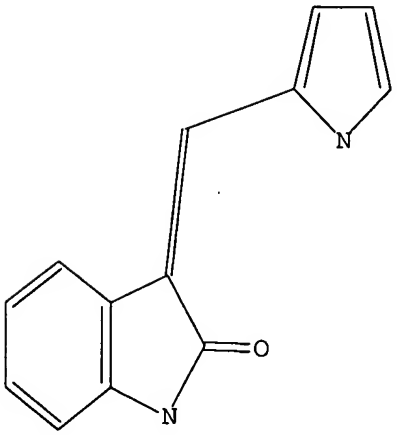
chain nodes :
15 16
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
5-15 9-16 11-16
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :
5-6 5-15 6-7 10-11 10-14
exact bonds :
5-9 8-9 9-16 11-12 11-16 12-13 13-14
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8
isolated ring systems :
containing 1 : 10 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS

L8 STRUCTURE UPLOADED

=> d l8
L8 HAS NO ANSWERS
L8 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l8
SAMPLE SEARCH INITIATED 14:39:00 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      223 TO ITERATE

100.0% PROCESSED      223 ITERATIONS                    50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.09

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          3565 TO     5355
PROJECTED ANSWERS:             1778 TO     3102

L9            50 SEA SSS SAM L8

=> s l8 sss full
FULL SEARCH INITIATED 14:39:19 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     4747 TO ITERATE

100.0% PROCESSED     4747 ITERATIONS                  2581 ANSWERS
SEARCH TIME: 00.00.01

L10         2581 SEA SSS FUL L8

=> FIL HCAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             167.38     342.56

FILE 'HCAPLUS' ENTERED AT 14:39:27 ON 07 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 7 Mar 2006 VOL 144 ISS 11
FILE LAST UPDATED: 6 Mar 2006 (20060306/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> d his

     (FILE 'HOME' ENTERED AT 14:35:32 ON 07 MAR 2006)

     FILE 'REGISTRY' ENTERED AT 14:35:54 ON 07 MAR 2006
L1                STRUCTURE UPLOADED
L2              3 S L1
L3             76 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 14:36:41 ON 07 MAR 2006
L4              1 S L3
L5                STRUCTURE UPLOADED
                  S L5

     FILE 'REGISTRY' ENTERED AT 14:38:08 ON 07 MAR 2006
L6             50 S L5

     FILE 'HCAPLUS' ENTERED AT 14:38:09 ON 07 MAR 2006
L7             26 S L6

     FILE 'REGISTRY' ENTERED AT 14:38:18 ON 07 MAR 2006
L8                STRUCTURE UPLOADED
L9             50 S L8
L10          2581 S L8 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 14:39:27 ON 07 MAR 2006

=> s l10
L11          427 L10

=> s l11 and kinase
          258792 KINASE
           50922 KINASES
          267146 KINASE
                   (KINASE OR KINASES)
L12          275 L11 AND KINASE

=> s l12 and protein
         1842070 PROTEIN
         1288156 PROTEINS
         2143577 PROTEIN
                   (PROTEIN OR PROTEINS)
L13          160 L12 AND PROTEIN
```

```
=> s l13 and transduction
        184441 TRANSDUCTION
           369 TRANSDUCTIONS
        184581 TRANSDUCTION
                  (TRANSDUCTION OR TRANSDUCTIONS)
L14         39 L13 AND TRANSDUCTION

=> s l14 and signal
        457885 SIGNAL
        151317 SIGNALS
        554815 SIGNAL
                  (SIGNAL OR SIGNALS)
L15         39 L14 AND SIGNAL

=> d l15 ibib abs tot

L15  ANSWER 1 OF 39  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1126626  HCAPLUS
DOCUMENT NUMBER:          143:399869
TITLE:                    Methods using VEGF signaling inhibitors for preventing
                          UVB-induced skin damage
INVENTOR(S):              Detmar, Michael; Hirakawa, Satoshi; Fujii, Seishiro
PATENT ASSIGNEE(S):       The General Hospital Corporation, USA
SOURCE:                   PCT Int. Appl., 36 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2005097187         A2    20051020    WO 2005-US11297          20050401
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     US 2005281761         A1    20051222    US 2005-96451            20050401
PRIORITY APPLN. INFO.:                       US 2004-559300P      P   20040401
AB   Skin damage, e.g. acute UVB-induced skin damage, can be reduced in a
     subject by administering to a subject having, or at risk for, acute
     UVB-induced skin damage, an agent that inhibits VEGF signaling.

L15  ANSWER 2 OF 39  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1078247  HCAPLUS
DOCUMENT NUMBER:          143:360086
TITLE:                    Combinations of signal transduction
                          inhibitors
INVENTOR(S):              Eck, Stephen Louis; Fry, David William; Leopold,
                          Judith Ann
PATENT ASSIGNEE(S):       Pfizer Inc, USA
```

SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005222163	A1	20051006	US 2005-95442	20050330
WO 2005094830	A1	20051013	WO 2005-IB720	20050318

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-557623P P 20040330

AB The present invention relates to methods for treating cancer comprising utilizing a combination of **signal transduction** inhibitors. More specifically, the present invention relates to combinations of so called cell cycle inhibitors with mitogen stimulated **kinase signal transduction** inhibitors, more specifically combinations of CDK inhibitors with mitogen stimulated **kinase signal transduction** inhibitors, more preferably MEK inhibitors. Other embodiments of the invention relate to addnl. combinations of the aforesaid combinations with standard anti-cancer agents such as cytotoxic agents, palliatives and antiangiogenics. Most specifically this invention relates to combinations of 6-acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-yl-pyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one including salt forms, which is a selective cyclin-dependent **kinase** 4 (CDK4) inhibitor, in combination with one or more MEK inhibitors, most preferably N-[(R)-2,3-dihydroxy-propoxy]-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide. The aforementioned combinations are useful for treating inflammation and cell proliferative diseases such as cancer and restenosis.

L15 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:570817 HCAPLUS
DOCUMENT NUMBER: 143:90995
TITLE: Compositions using CDK4 inhibitors for the treatment of mutant receptor tyrosine **kinase**-driven cellular proliferative diseases
INVENTOR(S): Briesewitz, Roger
PATENT ASSIGNEE(S): Theravance, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005058341 A2 20050630 WO 2004-US41333 20041209
WO 2005058341 A3 20051208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2005171182 A1 20050804 US 2004-8746 20041209
PRIORITY APPLN. INFO.: US 2003-528617P P 20031211

AB Uses are provided of a CDK4 inhibitor in the manufacture of a medicament for treating a subject suffering from a cellular proliferative disease characterized by the presence of a mutant receptor tyrosine **kinase**. The CDK4 inhibitor is for administration either alone or in combination with at least one of an inhibitor of the mutant receptor tyrosine **kinase** and an MEK inhibitor. Also provided are compns., including pharmaceutical formulations and kits thereof, comprising the above inhibitors.

L15 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:416371 HCAPLUS
DOCUMENT NUMBER: 143:1108
TITLE: Inhibition of neuronal apoptosis by the cyclin-dependent **kinase** inhibitor GW8510: Identification of 3' substituted indolones as a scaffold for the development of neuroprotective drugs
AUTHOR(S): Johnson, Kyle; Liu, Li; Majdzadeh, Nazanin; Chavez, Cindy; Chin, Paul C.; Morrison, Brad; Wang, Lulu; Park, Jane; Chugh, Priti; Chen, Hsin-Mei; D'Mello, Santosh R.
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of Texas at Dallas, Richardson, TX, USA
SOURCE: Journal of Neurochemistry (2005), 93(3), 538-548
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Increasing evidence suggests that neuronal apoptosis is triggered by the inappropriate activation of cyclin-dependent **kinases** leading to an abortive re-entry of neurons into the cell cycle. Pharmacol. inhibitors of cell-cycle progression may therefore have value in the treatment of neurodegenerative diseases in humans. GW8510 is a 3' substituted indolone that was developed recently as an inhibitor of cyclin-dependent **kinase** 2 (CDK2). We found that GW8510 inhibits the death of cerebellar granule neurons caused by switching them from high potassium (HK) medium to low potassium (LK) medium. Although GW8510 inhibits CDK2 and other CDKs when tested in in vitro biochem. assays, when used on cultured neurons it only inhibits CDK5, a cytoplasmic CDK that is not associated with cell-cycle progression. Treatment of cultured HEK293T cells with GW8510 does not inhibit cell-cycle progression, consistent with its inability to inhibit mitotic CDKs in intact cells. Neuroprotection by GW8510 is independent of Akt and MEK-ERK signaling. Furthermore, GW8510 does not block the LK-induced activation of Gsk3β and, while inhibiting c-jun phosphorylation, does not inhibit the increase in c-jun

expression observed in apoptotic neurons. We also examined the effectiveness of other 3' substituted indolone compds. to protect against neuronal apoptosis. We found that like GW8510, the VEGF Receptor 2 **Kinase** Inhibitors [3-(1H-pyrrol-2-ylmethylene)-1,3-dihydroindol-2-one], (Z)-3-2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-ylmethylidenylindol-2-one and [(Z)-5-Bromo-3-(4,5,6,7-tetrahydro-1H-indol-2-ylmethylene)-1,3-dihydroindol-2-one], the Src family **kinase** inhibitor SU6656 and a com. available inactive structural analog of an RNA-dependent **protein kinase** inhibitor 5-Chloro-3-(3,5-dichloro-4-hydroxybenzylidene)-1,3-dihydro-indol-2-one, are all neuroprotective when tested on LK-treated neurons. Along with our recent identification of the c-Raf inhibitor GW5074 (also a 3' substituted indolone) as a neuroprotective compound, our findings identify the 3' substituted indolone as a core structure for the designing of neuroprotective drugs that may be used to treat neurodegenerative diseases in humans.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:371491 HCAPLUS
DOCUMENT NUMBER: 142:423817
TITLE: Anti-vascular and anti-proliferation methods, therapies, and combinations employing specific tyrosine **kinase** inhibitors
INVENTOR(S): Nesbit, Mark; Spada, Alfred P.; He, Wei; Myers, Michael R.
PATENT ASSIGNEE(S): Gencell Sas, Fr.; Aventis Pharmaceuticals Inc.
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005038465	A2	20050428	WO 2004-EP12185	20041007
WO 2005038465	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-508859P P 20031007
OTHER SOURCE(S): MARPAT 142:423817

AB This invention is directed to potent inhibitors of **protein** tyrosine **kinase** such as quinoline/quinoxaline compds. alone or in synergistic combination with antiangiogenic or chemotherapeutic agents for the abrogation of mature vasculature within chemotherapeutic refractory tumors, pharmaceutical compns. comprising these compds., and to the use of these compds. for treating a patient suffering from or subject to disorders/conditions involving cell proliferation, and particularly treatment of brain cancer, ovarian cancer, pancreatic cancer prostate

cancer, and human leukemias, such as chronic myelogenous leukemia, acute myelogenous leukemia or acute lymphoid leukemia.

L15 ANSWER 6 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:371085 HCAPLUS
DOCUMENT NUMBER: 142:423814
TITLE: Combination therapy for cancer and viral infections
INVENTOR(S): Moller, Niels Peter Hundahl; Skak, Kresten; Mueller, Jorn Roland
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037306	A1	20050428	WO 2004-DK683	20041008

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
DK 2003-1529	A	20031017
US 2003-513422P	P	20031022
DK 2004-707	A	20040504
US 2004-569566P	P	20040510

AB The invention provides combination treatments with IL-21, analogs and derivs. thereof for the treatment of cancer and viral infection.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:369248 HCAPLUS
DOCUMENT NUMBER: 142:428777
TITLE: Antibodies of fibroblast growth factor receptor-1 and uses as inhibitors for the treatment of obesity
INVENTOR(S): Sun, Haijun
PATENT ASSIGNEE(S): Imclone Systems Incorporated, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037235	A2	20050428	WO 2004-US34970	20041018
WO 2005037235	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-512255P P 20031016

AB The present invention is directed to an antibody or fragments thereof that are specific for a fibroblast growth factor receptor (FGFR)-1(IIIb), FGFR-1(IIIc), and/or FGFR-4. Also, provided herein, are vectors and host cells comprising the nucleic acids encoding those antibodies. The present invention further provides methods of antagonizing FGFR-1 or FGFR-4 as a treatment for obesity, diabetes, or a condition related thereto, and methods of reducing food intake.

L15 ANSWER 8 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:296123 HCAPLUS
DOCUMENT NUMBER: 143:145911
TITLE: Disruption of fibroblast growth factor **signal** pathway inhibits the growth of synovial sarcomas: potential application of **signal** inhibitors to molecular target therapy
AUTHOR(S): Ishibe, Tatsuya; Nakayama, Tomitaka; Okamoto, Takeshi; Aoyama, Tomoki; Nishijo, Koichi; Shibata, Kotaro Roberts; Shima, Yasuko; Nagayama, Satoshi; Katagiri, Toyomasa; Nakamura, Yusuke; Nakamura, Takashi; Toguchida, Junya
CORPORATE SOURCE: Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan
SOURCE: Clinical Cancer Research (2005), 11(7), 2702-2712 CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synovial sarcoma is a soft tissue sarcoma, the growth regulatory mechanisms of which are unknown. We investigated the involvement of fibroblast growth factor (FGF) **signals** in synovial sarcoma and evaluated the therapeutic effect of inhibiting the FGF **signal.** The expression of 22 FGF and 4 FGF receptor (FGFR) genes in 18 primary tumors and five cell lines of synovial sarcoma were analyzed by reverse transcription-PCR. Effects of recombinant FGF2, FGF8, and FGF18 for the activation of mitogen-activated **protein kinase** (MAPK) and the growth of synovial sarcoma cell lines were analyzed. Growth inhibitory effects of FGFR inhibitors on synovial sarcoma cell lines were investigated in vitro and in vivo. Synovial sarcoma cell lines expressed multiple FGF genes especially those expressed in neural tissues, among which FGF8 showed growth stimulatory effects in all synovial sarcoma cell lines. FGF **signals** in synovial sarcoma induced the phosphorylation of extracellular **signal**-regulated **kinase** (ERK1/2) and p38MAPK but not c-Jun NH2-terminal **kinase.** Disruption of the FGF signaling pathway in synovial sarcoma by specific inhibitors of FGFR caused cell cycle arrest leading to significant growth inhibition both in vitro and in vivo. Growth inhibition by the FGFR inhibitor was associated with a down-regulation of phosphorylated ERK1/2 but not p38MAPK, and an ERK **kinase** inhibitor also showed growth inhibitory effects for

synovial sarcoma, indicating that the growth stimulatory effect of FGF was transmitted through the ERK1/2. FGF **signals** have an important role in the growth of synovial sarcoma, and inhibitory mols. will be of potential use for mol. target therapy in synovial sarcoma.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283363 HCAPLUS
DOCUMENT NUMBER: 142:329832
TITLE: Combination of a vegf receptor inhibitor with a chemotherapeutic agent
INVENTOR(S): Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry Min-Jian; Kinder, Frederick Ray, Jr.; Lane, Heidi; Latour, Elisabeth Jeanne; Manley, Paul William; Wood, Jeanette Marjorie
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027972	A2	20050331	WO 2004-EP10686	20040923
WO 2005027972	A3	20051103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505250P P 20030923

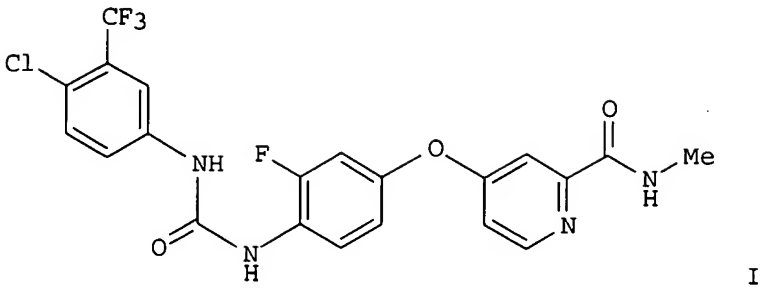
AB The present invention relates to a combination therapy for treating patients suffering from proliferative diseases or diseases associated with persistent angiogenesis. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: an aromatase inhibitor; an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist; a topoisomerase I inhibitor or a topoisomerase II inhibitor; a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound; a compound targeting/decreasing a **protein** or lipid **kinase** activity or a **protein** or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes. The patient is treated with :(a) a VEGF inhibitor compound;and (b) one or more chemotherapeutic agents selected from the group consisting of : a bradykinin 1 receptor or an angiotensin II antagonist ; a cyclooxygenase inhibitor , a bisphosphonate , a heparanase inhibitor (prevents heparan sulfate degradation) , e.g. , PI-88 , a biol. response modifier, preferably a lymphokine or interferons , e.g., interferon γ, an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways ; an

inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor ; a telomerase inhibitor , e.g. , telomestatin ; a protease inhibitor, a matrix metalloproteinase inhibitor , a methionine aminopeptidase inhibitor , e.g. , bengamide or a derivative thereof , or a proteasome inhibitor , e. g. , PS-341. The patient is treated with : (a) a VEGF inhibitor compound (b) one or more chemotherapeutic agents selected from the group consisting of : agents used in the treatment of hematol. malignancies or FMS-like tyrosine **kinase** inhibitors ; an HSP90 inhibitors ; HDAC inhibitors ; mTOR inhibitors ; somatostatin receptor antagonists ; integrin antagonists ; anti-leukemic compds. ; tumor cell damaging approaches such as ionizing radiation EDG binders ; anthranilic acid amide class of **kinase** inhibitors ; ribonucleotide reductase inhibitors ; S-adenosylmethionine decarboxylase inhibitors ; antibodies against VEGF or VEGFR ; photodynamic therapy ; angiostatic steroids ; implants containing corticosteroids ; AT1 receptor antagonists ; ACE inhibitors.

L15 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:99470 HCAPLUS
DOCUMENT NUMBER: 142:197889
TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 **kinase**-mediated diseases
INVENTOR(S): Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, Scott
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009961	A2	20050203	WO 2004-US23500	20040722
WO 2005009961	A3	20050331		
WO 2005009961	B1	20050602		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005038080	A1	20050217	US 2004-895985	20040722
PRIORITY APPLN. INFO.:			US 2003-489102P P	20030723
			US 2004-540326P P	20040202

GI



I

AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine **kinase** with IC50 = 83nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

L15 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:82083 HCAPLUS
DOCUMENT NUMBER: 142:328670
TITLE: FLT3 **signal transduction** inhibitors as molecular-targeted drugs
AUTHOR(S): Kiyoi, Hitoshi; Naoe, Tomoki
CORPORATE SOURCE: School of Medicine, Nagoya University, Japan
SOURCE: Chiryogaku (2004), 38(12), 1323-1326
CODEN: CHRYDT; ISSN: 0386-8109
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. FLT3 **signal transduction** inhibitors as mol.-targeted drugs in the treatment of acute myeloid leukemia and acute lymphoid leukemia is reviewed including FLT3 **kinase** inhibitors such as MLN-518, PKC-412, CEP-701, and SU11248 etc. as well as anti FLT3 antibody, and HSP90 inhibitors as examples.

L15 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902199 HCAPLUS
DOCUMENT NUMBER: 141:374704
TITLE: Composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders
INVENTOR(S): Chang, Yan; Sasak, Vodek
PATENT ASSIGNEE(S): Glycogenesys, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091634	A1	20041028	WO 2004-US10675	20040407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004023925	A1	20040205	US 2003-408723	20030407
CA 2521649	AA	20041028	CA 2004-2521649	20040407
US 2004223971	A1	20041111	US 2004-819901	20040407
EP 1617849	A1	20060125	EP 2004-759200	20040407

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.:

US 2003-408723	A	20030407
US 2003-461006P	P	20030407
US 2003-474562P	P	20030530
US 2001-299991P	P	20010621
US 2002-176235	A2	20020620
WO 2004-US10675	W	20040407

AB The present invention is directed to methods and compns. for augmenting treatment of cancers and other proliferative disorders. In particular embodiments, the invention combines the administration of an agent that inhibits the anti-apoptotic activity of galectin-3 (e.g., a 'galectin-3 inhibitor') so as to potentiate the toxicity of a chemotherapeutic agent. In certain preferred embodiments, the conjoint therapies of the present invention can be used to improve the efficacy of those chemotherapeutic agents whose cytotoxicity is influenced by the status of an anti-apoptotic Bcl-2 **protein** for the treated cell. For instance, galectin-3 inhibitors can be administered in combination with a chemotherapeutic agent that interferes with DNA replication fidelity or cell-cycle progression of cells undergoing unwanted proliferation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:834491 HCAPLUS
DOCUMENT NUMBER: 141:360313
TITLE: SU5416 inhibited VEGF and HIF-1α expression through the PI3K/AKT/p70S6K1 signaling pathway
AUTHOR(S): Zhong, Xiao-Song; Zheng, Jenny Z.; Reed, Eddie; Jiang, Bing-Hua
CORPORATE SOURCE: Mary Babb Randolph Cancer Center, Department of Microbiology, Immunology and Cell Biology, West Virginia University, Morgantown, WV, 26506-9300, USA
SOURCE: Biochemical and Biophysical Research Communications (2004), 324(2), 471-480
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ovarian cancer has the highest mortality rate of any gynecol. disease affecting women in Western countries. VEGF is a crucial inducer of angiogenesis both in vivo and in vitro. VEGF is commonly upregulated in ovarian cancer and is regulated by HIF-1. SU5416 is known to inhibit various stages of tumor growth. In this study, we show that SU5416 inhibited VEGF mRNA expression in ovarian cancer cells in a dose-dependent manner. SU5416 inhibited VEGF expression at the transcriptional level through the HIF-1 DNA binding site. HIF-1 is composed of HIF-1α and

HIF-1β subunits. SU5416 specifically decreased HIF-1α, but not HIF-1β **protein** levels. To understand the signaling pathways regulating SU5416-inhibited VEGF and HIF-1α expression, we found that SU5416 inhibited PI3K activity. AKT is a downstream target of PI3K. We found that SU5416 also inhibited AKT and p70S6K1 activation and activity in a dose-dependent manner. These results demonstrate that SU5416 inhibited VEGF and HIF-1α expression through the inhibition of PI3K/AKT/p70S6K1 pathway in ovarian cancer cells. These results indicate that SU5416 may be an effective agent for ovarian cancer treatment through the inhibition of VEGF and HIF-1 expression, and the activation of PI3K/AKT/p70S6K1 signaling pathway.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:452980 HCAPLUS
DOCUMENT NUMBER: 141:33766
TITLE: Methods for assessing the anti-cancer activity of a KIT tyrosine **kinase** inhibitor, gastrointestinal stromal tumor treatment, and assessing cancer progression, using gene expression profiling
INVENTOR(S): Eisenberg, Burton; Von Mehren, Margaret; Frolov, Andrey; Godwin, Andrew
PATENT ASSIGNEE(S): Fox Chase Cancer Center, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045545	A2	20040603	WO 2003-US36820	20031118
WO 2004045545	A3	20040812		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-427326P P 20021118

AB The present invention provides novel methods for the treatment of cancer, methods for screening compds. having anti-cancer activity, and methods of assessing cancer progression. In accordance with the present invention, a method of assessing the anti-cancer activity of a KIT tyrosine **kinase** inhibitor in a biol. sample comprising a tumor cell is provided. In a preferred embodiment, the tumor is a gastrointestinal stromal tumor (GIST) and the KIT tyrosine **kinase** inhibitor is imatinib, SU11248 (Sugen Pharmaceuticals), or a pharmaceutically acceptable salt thereof. DNA microarrays revealed 148 genes that were differentially expressed between untreated and imatinib-treated human GIST cells, in vitro. One of these genes, Sprouty4A (SPRY4A) a regulator of tyrosine **kinase**-mediated signaling pathways, was dramatically

down- regulated. A biomarker MAFbx was up-regulated in response to imatinib treatment. In addition, imatinib inhibited KIT phosphorylation without affecting the total level of KIT **protein.** The inventors proposed a method for determining the efficacy of an anticancer treatment comprising detection of an alteration in phosphorylation of a biomarker (such as decrease in GAB1 phosphorylation).

L15 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:419904 HCAPLUS
DOCUMENT NUMBER: 142:70669
TITLE: Characterization of a Conserved Structural Determinant Controlling **Protein Kinase** Sensitivity to Selective Inhibitors
AUTHOR(S): Blencke, Stephanie; Zech, Birgit; Engkvist, Ola; Greff, Zoltan; Orfi, Laszlo; Horvath, Zoltan; Keri, Gyoergy; Ullrich, Axel; Daub, Henrik
CORPORATE SOURCE: Axxima Pharmaceuticals AG, Munchen, 81377, Germany
SOURCE: Chemistry & Biology (2004), 11(5), 691-701
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Some **protein kinases** are known to acquire resistance to selective small mol. inhibitors upon mutation of a conserved threonine at the ATP binding site to a larger residue. Here, we performed a comprehensive mutational anal. of this structural element and determined the cellular sensitivities of several disease-relevant tyrosine **kinases** against various inhibitors. Mutant **kinases** possessing a larger side chain at the critical site showed resistance to most compds. tested, such as ZD1839, PP1, AG1296, STI571, and a pyrido[2,3-d]pyrimidine inhibitor. In contrast, indolinones affected both wild-type and mutant **kinases** with similar potencies. Resistant mutants were established for pharmacol. anal. of βPDGF receptor-mediated signaling and allowed the generation of a drug-inducible system of cellular Src **kinase** activity. Our data establish a conserved structural determinant of **protein kinase** sensitivity relevant for both **signal transduction** research and drug development.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:256840 HCAPLUS
DOCUMENT NUMBER: 140:417435
TITLE: Preclinical studies of fibroblast growth factor receptor 3 as a therapeutic target in multiple myeloma
AUTHOR(S): Paterson, Joshua L.; Li, Zhihua; Wen, Xiao-Yan; Masih-Khan, Esther; Chang, Hong; Pollett, Jonathan B.; Trudel, Suzanne; Stewart, A. Keith
CORPORATE SOURCE: Institute of Medical Science, University of Toronto, Toronto, ON, Can.
SOURCE: British Journal of Haematology (2004), 124(5), 595-603
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dysregulation of fibroblast growth factor receptor 3 (FGFR3) by the translocation t(4;14)(p16;q32) occurs in 15% of multiple myeloma (MM) patients and confers a growth and survival advantage to malignant plasma

cells. As FGFR3 is a mol. target, we assessed the therapeutic potential of the FGFR-specific tyrosine **kinase** inhibitors SU5402 and SU10991 in MM. SU5402 inhibited FGFR3 phosphorylation in vitro and in murine MM tumor models. B cells dependent on FGFR3 for survival were specifically sensitive to SU5402. A panel of 11 human myeloma cell lines was studied, five bearing the t(4;14) translocation. The KMS11 human myeloma cell line, which expresses constitutively active mutant FGFR3, displayed an 85% decrease in S-phase cells, a 95% increase in G0/G1 cells, and 4·5-fold increase in apoptotic cells after 72 h treatment with 10 μmol/l SU5402. Activated extracellular **signal**-regulated **kinases** 1 and 2 and **signal** transducer and activator of transcription 3 were rapidly down-regulated after SU5402 treatment. In human myeloma cell lines expressing wild-type FGFR3 the stimulating effect of aFGF ligand was abrogated by SU5402 treatment. Myeloma cells lacking the t(4;14) or with the t(4;14) and a secondary RAS mutation did not respond to therapy. These findings support the development of clin. trials of early intervention with FGFR3 inhibitors in t(4;14) myeloma.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:234002 HCAPLUS
DOCUMENT NUMBER: 140:350175
TITLE: Mutations in the tyrosine **kinase** domain of FLT3 define a new molecular mechanism of acquired drug resistance to PTK inhibitors in FLT3-ITD-transformed hematopoietic cells
AUTHOR(S): Bagrintseva, Ksenia; Schwab, Ruth; Kohl, Tobias M.; Schnittger, Susanne; Eichenlaub, Sabine; Ellwart, Joachim W.; Hiddemann, Wolfgang; Spiekermann, Karsten
CORPORATE SOURCE: Department of Medicine III, University Hospital Grosshadem, Clinical Cooperative Group "Leukemia," GSF-National Research Center for Environment and Health, Institute of Molecular Immunology, Ludwig-Maximilians University, Munich, Germany
SOURCE: Blood (2004), 103(6), 2266-2275
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activating mutations in the juxtamembrane domain (FLT3-length mutations, FLT3-LM) and in the **protein** tyrosine **kinase** domain (TKD) of FLT3 (FLT3-TKD) represent the most frequent genetic alterations in acute myeloid leukemia (AML) and define a mol. target for therapeutic interventions by **protein** tyrosine **kinase** (PTK) inhibitors. We could show that distinct activating FLT3-TKD mutations at position D835 mediate primary resistance to FLT3 PTK inhibitors in FLT3-transformed cell lines. In the presence of increasing concns. of the FLT3 PTK inhibitor SU5614, we generated inhibitor resistant Ba/F3 FLT3-internal tandem duplication (ITD) cell lines (Ba/F3 FLT3-ITD-R1-R4) that were characterized by a 7- to 26-fold higher IC50 (concentration that inhibits 50%) to SU5614 compared with the parental ITD cells. The mol. characterization of ITD-R1-4 cells demonstrated that specific TKD mutations (D835N and Y842H) on the ITD background were acquired during selection with SU5614. Introduction of these dual ITD-TKD, but not single D835N or Y842H FLT3 mutants, in Ba/F3 cells restored the FLT3 inhibitor resistant phenotype. Our data show that preexisting or acquired mutations in the PTK domain of FLT3 can induce drug resistance to FLT3 PTK inhibitors in vitro. These findings provide a mol. basis for the

evaluation of clin. resistance to FLT3 PTK inhibitors in patients with AML.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:100803 HCAPLUS
DOCUMENT NUMBER: 140:139483
TITLE: Method for enhancing the effectiveness of therapies of hyperproliferative diseases
INVENTOR(S): Chang, Yan; Sasak, Vodek
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 176,235.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004023925	A1	20040205	US 2003-408723	20030407
US 2003013681	A1	20030116	US 2002-176235	20020620
US 6680306	B2	20040120		
CN 1543351	A	20041103	CN 2002-816003	20020621
US 2004043962	A1	20040304	US 2003-657383	20030908
CA 2521649	AA	20041028	CA 2004-2521649	20040407
WO 2004091634	A1	20041028	WO 2004-US10675	20040407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1617849	A1	20060125	EP 2004-759200	20040407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.:

US 2001-299991P	P	20010621
US 2002-176235	A2	20020620
US 2003-408723	A	20030407
US 2003-461006P	P	20030407
US 2003-474562P	P	20030530
WO 2004-US10675	W	20040407

AB The efficacy of conventional cancer therapies such as surgery, chemotherapy and radiation is enhanced by the use of a therapeutic material which binds to and interacts with galectins. The therapeutic material can enhance apoptosis thereby increasing the effectiveness of oncolytic agents. It can also inhibit angiogenesis thereby moderating tumor growth and/or metastasis.

L15 ANSWER 19 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:931518 HCAPLUS
DOCUMENT NUMBER: 140:689

TITLE: Genes showing altered patterns of expression in response to inhibition of tyrosine **kinases** and their use in screening **kinase** inhibitors
INVENTOR(S): Morimoto, Alyssa; Deprimo, Samuel; O'Farrell, Anne-Marie; Smolich, Beverly D.; Manning, William C.; Walter, Sarah A.; Schilling, James Walter, Jr.; Cherrington, Julie
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 408 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097854	A2	20031127	WO 2003-US15711	20030519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004018528	A1	20040129	US 2003-440464	20030519
PRIORITY APPLN. INFO.:			US 2002-380872P P	20020517
			US 2003-448874P P	20030224
			US 2003-448922P P	20030224

OTHER SOURCE(S): MARPAT 140:689
AB Genes that are regulated by tyrosine **kinase**-dependent **signal transduction** pathways are identified as markers for the screening of inhibitors of **kinase** activity. The change in levels of either the **protein** or mRNA in a suitable test system may be used to assess the effectiveness of a test compound as an inhibitor of a tyrosine **kinase** activity. The invention also relates to novel methods, wherein a change in the level of at least one biomarker in a mammal exposed to a compound, compared to the level of the biomarker(s) in a mammal that has not been exposed to the compound, indicates whether the mammal is being exposed to, or is experiencing or will experience a therapeutic or toxic effect in response to, a compound that inhibit tyrosine **kinase** activity.

L15 ANSWER 20 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:885660 HCAPLUS
DOCUMENT NUMBER: 140:174631
TITLE: A selective small molecule inhibitor of c-Met **kinase** inhibits c-Met-dependent phenotypes in vitro and exhibits cytoreductive antitumor activity in vivo
AUTHOR(S): Christensen, James G.; Schreck, Randall; Burrows, Jon; Kuruganti, Poonam; Chan, Emily; Le, Phuong; Chen, Jeffrey; Wang, Xueyan; Ruslim, Lany; Blake, Robert; Lipson, Kenneth E.; Ramphal, John; Do, Steven; Cui, Jingrong J.; Cherrington, Julie M.; Mendel, Dirk B.
CORPORATE SOURCE: Preclinical Research and Exploratory Development,

SUGEN, Inc., South San Francisco, CA, 94080, USA
SOURCE: Cancer Research (2003), 63(21), 7345-7355
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The c-Met receptor tyrosine **kinase** and its ligand, hepatocyte growth factor (HGF), have been implicated in the development and progression of several human cancers and are attractive targets for cancer therapy. PHA-665752 was identified as a small mol., ATP-competitive, active-site inhibitor of the catalytic activity of c-Met **kinase** (Ki 4 nM). PHA-665752 also exhibited >50-fold selectivity for c-Met compared with a panel of diverse tyrosine and serine-threonine **kinases.** In cellular studies, PHA-665752 potently inhibited HGF-stimulated and constitutive c-Met phosphorylation, as well as HGF and c-Met-driven phenotypes such as cell growth (proliferation and survival), cell motility, invasion, and/or morphol. of a variety of tumor cells. In addition, PHA-665752 inhibited HGF-stimulated or constitutive phosphorylation of mediators of downstream **signal transduction** of c-Met, including Gab-1, extracellular regulated **kinase**, Akt, **signal** transducer and activator of transcription 3, phospholipase C γ, and focal adhesion **kinase**, in multiple tumor cell lines in a pattern correlating to the phenotypic response of a given tumor cell. In in vivo studies, a single dose of PHA-665752 inhibited c-Met phosphorylation in tumor xenografts for up to 12 h. Inhibition of c-Met phosphorylation was associated with dose-dependent tumor growth inhibition/growth delay over a repeated administration schedule at well-tolerated doses. Interestingly, potent cytoreductive activity was demonstrated in a gastric carcinoma xenograft model. Collectively, these results demonstrate the feasibility of selectively targeting c-Met with ATP-competitive small-mols. and suggest the therapeutic potential of targeting c-Met in human cancers.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 21 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:733795 HCAPLUS
DOCUMENT NUMBER: 140:174580
TITLE: A Novel Small Molecule Met Inhibitor Induces Apoptosis in Cells Transformed by the Oncogenic TPR-MET Tyrosine **Kinase**
AUTHOR(S): Sattler, Martin; Pride, Yuri B.; Ma, Patrick; Gramlich, Jessica L.; Chu, Stephanie C.; Quinnan, Laura A.; Shirazian, Sheri; Liang, Congxin; Podar, Klaus; Christensen, James G.; Salgia, Ravi
CORPORATE SOURCE: Department of Medical Oncology, Department of Medicine, Dana-Farber Cancer Institute, Harvard Medical School, Brigham and Women's Hopital, Boston, MA, 02115, USA
SOURCE: Cancer Research (2003), 63(17), 5462-5469
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Met receptor tyrosine **kinase** has been shown to be overexpressed or mutated in a variety of solid tumors and has, therefore, been identified as a good candidate for molecularly targeted therapy. Activation of the Met tyrosine **kinase** by the TPR gene was originally described in vitro through carcinogen-induced rearrangement.

The TPR-MET fusion **protein** contains constitutively elevated Met tyrosine **kinase** activity and constitutes an ideal model to study the transforming activity of the Met **kinase.** We found, when introduced into an interleukin 3-dependent cell line, TPR-MET induces factor independence and constitutive tyrosine phosphorylation of several cellular **proteins.** One major tyrosine phosphorylated **protein** was identified as the TPR-MET oncoprotein itself. Inhibition of the Met **kinase** activity by the novel small mol. drug SU11274 [(3Z)-N-(3-chlorophenyl)-3-({3,5-dimethyl-4-[(4-methylpiperazin-1-yl)carbonyl]-1H-pyrrol-2-yl}methylene)-N-methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonamide] led to time- and dose-dependent reduced cell growth. The inhibitor did not affect other tyrosine **kinase** oncoproteins, including BCR-ABL, TEL-JAK2, TEL-PDGFβR, or TEL-ABL. The Met inhibitor induced G1 cell cycle arrest and apoptosis with increased Annexin V staining and caspase 3 activity. The autophosphorylation of the Met **kinase** was reduced on sites that have been shown previously to be important for activation of pathways involved in cell growth and survival, especially the phosphatidylinositol-3'-**kinase** and the Ras pathway. In particular, we found that the inhibitor blocked phosphorylation of AKT, GSK-3β, and the pro-apoptotic transcription factor FKHR. The characterization of SU11274 as an effective inhibitor of Met tyrosine **kinase** activity illustrates the potential of targeting for Met therapeutic use in cancers associated with activated forms of this **kinase.**

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 22 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:355612 HCAPLUS
DOCUMENT NUMBER: 138:362649
TITLE: Treatment of cancer with anti-ErbB2 antibodies
INVENTOR(S): Sliwkowski, Mark X.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 56 pp., Cont.-in-part of U.S. Ser. No. 602,812.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003086924	A1	20030508	US 2002-268501	20021010
US 6949245	B1	20050927	US 2000-602812	20000623
US 2004013667	A1	20040122	US 2003-608626	20030627
US 2005208043	A1	20050922	US 2005-44749	20050127
US 2005238640	A1	20051027	US 2005-154465	20050616
US 2006034842	A1	20060216	US 2005-223361	20050909
PRIORITY APPLN. INFO.:			US 1999-141316P	P 19990625
			US 2000-602812	A2 20000623
			US 2002-268501	A2 20021010

AB The present application describes methods for treating cancer with anti-ErbB2 antibodies, such as anti-ErbB2 antibodies that block ligand activation of an ErbB receptor. Recombinant humanized monoclonal antibody 2C4 was effective in inhibiting breast cancer tumor growth in MCF7 xenografts.

L15 ANSWER 23 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:273837 HCAPLUS
DOCUMENT NUMBER: 139:345023
TITLE: Molecular Therapeutics: Is One Promiscuous Drug against Multiple Targets Better than Combinations of Molecule-specific Drugs?
AUTHOR(S): Arteaga, Carlos L.
CORPORATE SOURCE: Vanderbilt-Ingram Comprehensive Cancer Center, Departments of Medicine and Cancer Biology, and Breast Cancer Program, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SOURCE: Clinical Cancer Research (2003), 9(4), 1231-1232
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, discussing the benefits and disadvantages of two different approaches to mol.-targeted therapeutics, i.e., the use of promiscuous small mol. inhibitors acting against multiple targets, such as ZD6474, SU6668, or STI-571, vs. combinations of inhibitors, such as ZD1839, SC-236, and antisense oligonucleotide against **protein kinase** A type I that work together in an additive or synergistic way.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 24 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:888893 HCAPLUS
DOCUMENT NUMBER: 137:383800
TITLE: Chimeric and humanized antibodies and fragments specific to glycosylated EGF receptor for cancer diagnosis and therapy
INVENTOR(S): Old, Lloyd J.; Johns, Terrance Grant; Panousis, Con; Scott, Andrew Mark; Renner, Christoph; Ritter, Gerd; Jungbluth, Achim; Stockert, Elisabeth; Collins, Peter; Cavenee, Webster K.; Huang, Huei-Jen; Burgess, Anthony Wilks; Nice, Edouard Collins
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 245 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092771	A2	20021121	WO 2002-US15185	20020513
WO 2002092771	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2447139	AA	20021121	CA 2002-2447139	20020513

EP 1392359 A2 20040303 EP 2002-739258 20020513
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004531263 T2 20041014 JP 2002-589639 20020513
PRIORITY APPLN. INFO.: US 2001-290410P P 20010511
US 2001-326019P P 20010928
US 2001-342258P P 20011221
WO 2002-US15185 W 20020513

AB The invention relates to specific binding members, particularly antibodies and active fragments thereof, which recognize an aberrant post-translationally modified, particularly an aberrant glycosylated form of the EGFR. The binding members, particularly antibodies and fragments thereof, of the invention do not bind to EGFR on normal cells in the absence of amplification of the wild- type gene and are capable of binding the de2-7 EGFR at an epitope which is distinct from the junctional peptide. Antibodies of this type are exemplified by the novel antibody 806 whose VH and VL sequences are illustrated as SEQ ID Nos: 2 and 4 and chimeric antibodies thereof as exemplified by ch806. The antibodies may also be radiolabeled for immunodiagnosis and radioimmunotherapy of cancers, especially brain-resident cancers.

L15 ANSWER 25 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:805255 HCAPLUS
DOCUMENT NUMBER: 138:314076
TITLE: SU5416 and SU5614 inhibit **kinase** activity of wild-type and mutant FLT3 receptor tyrosine **kinase**
AUTHOR(S): Yee, Kevin W. H.; O'Farrell, Anne Marie; Smolich, Beverly D.; Cherrington, Julie M.; McMahon, Gerald; Wait, Cecily L.; McGreevey, Laura S.; Griffith, Diana J.; Heinrich, Michael C.
CORPORATE SOURCE: Department of Medicine, Division of Hematology and Medical Oncology, Portland Veterans Affairs Medical Center, Oregon Health and Science University, Portland, USA
SOURCE: Blood (2002), 100(8), 2941-2949
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Internal tandem duplication (ITd) in the juxtamembrane portion of Fms-like tyrosine **kinase** 3 (FLT3), a type III receptor tyrosine **kinase** (RTK), is the most common mol. defect associated with acute myeloid leukemia (AML). The high prevalence of this activating mutation makes it a potential target for molecularly based therapy. Indolinone tyrosine **kinase** inhibitors have known activity against KIT, another member of the type III RTK family. Given the conserved homol. between members of this family, we postulated that the activity of some KIT inhibitors would extend to FLT3. We used various leukemic cell lines (BaF3, MV 4-11, RS 4;11) to test the activity of indolinone compds. against the FLT3 **kinase** activity of both wild-type (WT) and ITD isoforms. Both SU5416 and SU5614 were capable of inhibiting autophosphorylation of ITD and WT FLT3 (SU5416 concentration that inhibits 50% [IC50], 100 nM; and SU5614 IC50 10 nM). FLT3-dependent activation of the downstream signaling **proteins** mitogen-activated **protein** **kinase** (MAPK) and **signal** transducer and activator of transcription 5 (STAT5) was also inhibited by treatment in the same concentration rages. FLT3 inhibition by SU5416 and SU5614 resulted in reduced

proliferation (IC50, 250 nM and 100 nM, resp.) and induction of apoptosis of FLT3 ITD-pos. leukemic cell lines. Treatment of these cells with an alternative growth factor (granulocyte-macrophage colony-stimulating factor [GM-CSF]) restored MAPK signaling and cellular proliferation, demonstrating specificity of the observed inhibitory effects. We conclude that SU5416 and SU5614 are potent inhibitors of FLT3. Our finding that inhibition of FLT3 induces apoptosis of leukemic cells supports the feasibility of targeting FLT3 as a novel treatment strategy for AML.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 26 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:805222 HCAPLUS
DOCUMENT NUMBER: 139:270353
TITLE: Inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine **kinase** inhibitors. [Erratum to document cited in CA138:147266]
AUTHOR(S): Liao, Albert T.; Chien, May B.; Shenoy, Narmada; Mendel, Dirk B.; McMahon, Gerald; Cherrington, Julie M.; London, Cheryl A.
CORPORATE SOURCE: Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California at Davis, Davis, CA, 95616, USA
SOURCE: Blood (2002), 100(8), 2696
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In "Materials and methods", under "Antibodies", the fifth sentence should refer to "anti-phosphatidyl inositol 3-**kinase.**".

L15 ANSWER 27 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:541364 HCAPLUS
DOCUMENT NUMBER: 138:147266
TITLE: Inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine **kinase** inhibitors
AUTHOR(S): Liao, Albert T.; Chien, May B.; Shenoy, Narmada; Mendel, Dirk B.; McMahon, Gerald; Cherrington, Julie M.; London, Cheryl A.
CORPORATE SOURCE: Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California at Davis, Davis, CA, 95616, USA
SOURCE: Blood (2002), 100(2), 585-593
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutations in the proto-oncogene c-kit, including point mutations, deletions, or duplications in the neg. regulatory juxtamembrane (JM) domain or point mutations in the catalytic domain, have been observed in human and canine cancers and often result in constitutive activation of Kit in the absence of ligand binding. To identify a receptor tyrosine **kinase** (RTK) inhibitor capable of blocking the function of mutant Kit, we evaluated 3 indolinones (SU11652, SU11654, and SU11655) that act as competitive inhibitors of ATP binding to several members of the split **kinase** family of RTKs, including VEGFR, FGFR, PDGFR, and Kit. Mast cell lines expressing either wildtype (WT) Kit, a point mutation in

the JM domain, a tandem duplication in the JM domain, or a point mutation in the catalytic domain were used for these studies. All 3 indolinones inhibited phosphorylation of WT Kit in the presence of stem cell factor at concns. as low as 0.01 μM. Autophosphorylation of both JM mutants was inhibited at 0.01 to 0.1 μM, resulting in cell cycle arrest within 24 h, whereas autophosphorylation of the catalytic domain mutant was inhibited at 0.25 to 0.5 μM, resulting in cell death within 24 h. Poly(ADP-ribose) polymerase (PARP) cleavage was noted in all Kit mutant lines after indolinone treatment. In summary, SU11652, SU11654, and SU11655 are effective RTK inhibitors capable of disrupting the function of all forms of mutant Kit. Because the concns. of drug necessary for receptor inhibition are readily achievable and nontoxic in vivo, these compds. may be useful in the treatment of spontaneous cancers expressing Kit mutations.

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 28 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:539677 HCAPLUS
DOCUMENT NUMBER: 137:109202
TITLE: Preparation of 4-aryl substituted indolinones as **protein kinase signal transduction** modulators for inhibiting abnormal cell proliferation
INVENTOR(S): Cui, Jingrong; Zhang, Ruofei; Shen, Hong; Chu, Ji Yu; Zhang, Fang-Jie; Koenig, Marcel; Do, Steven Huy; Li, Xiaoyuan; Wei, Chung Chen; Tang, Peng Cho
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 560 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055517	A2	20020718	WO 2001-US48564	20011220
WO 2002055517	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432114	AA	20020718	CA 2001-2432114	20011220
US 2003069297	A1	20030410	US 2001-23488	20011220
US 6677368	B2	20040113		
EP 1349852	A2	20031008	EP 2001-997065	20011220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004518669	T2	20040624	JP 2002-556186	20011220
US 2004157909	A1	20040812	US 2003-736243	20031216
US 6861418	B2	20050301		

PRIORITY APPLN. INFO.: US 2000-256479P P 200012

US 2001-23488 A3 20011220
WO 2001-US48564 W 20011220

OTHER SOURCE(S): MARPAT 137:109202
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = (un)substituted aryl or heteroaryl; R2 = H, halo, alkyl, alkenyl, alkynyl, heterocyclyl, etc.; R3 = (un)substituted pyrrole or cycloalkenylpyrrole], as well as pharmaceutical compns. thereof, are prepared and disclosed as compds. capable of modulating **protein kinase signal transduction** in order to regulate, modulate and/or inhibit abnormal cell proliferation. Thus II, was prepared via condensation of 4-phenyl-1,3-dihydroindol-2-one with 5-formyl-2-methyl-4-[3-(4-methylpiperazin-1-yl)propyl]-1H-pyrrole-3-carboxylic acid Et ester. I were evaluated against eight specfic **kinases**, e.g., FGFR1, for which I possessed IC50 values (μM) of 0.0091-2.07. The present invention also relates to methods for treating **protein kinase** related disorders.

L15 ANSWER 29 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:335839 HCAPLUS
DOCUMENT NUMBER: 137:241813
TITLE: ZD1839 (Iressa) induces antiangiogenic effects through inhibition of epidermal growth factor receptor tyrosine **kinase**
AUTHOR(S): Hirata, Akira; Ogawa, Soh-ichiro; Kometani, Takuro; Kuwano, Takashi; Naito, Seiji; Kuwano, Michihiko; Ono, Mayumi
CORPORATE SOURCE: Department of Medical Biochemistry, Graduate School of Medical Sciences, Kyushu University, Fukuoka, 812-8582, Japan
SOURCE: Cancer Research (2002), 62(9), 2554-2560
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epidermal growth factor receptor (EGFR) tyrosine **kinase** is a potential target for anticancer therapy. ZD1839 (Iressa) is a selective inhibitor of EGFR tyrosine **kinase.** In this study, we investigated the question as to whether the antitumor effect of ZD1839 is partly attributable to antiangiogenic activity and the potential mechanisms involved. Both ZD1839 and SU5416 [a vascular endothelial growth factor (VEGF)-receptor tyrosine **kinase** inhibitor] inhibited the migration of human umbilical vein endothelial cell cocultivated with EGF-stimulated cancer cells. ZD1839 also inhibited EGF-induced migration and the formation of tube-like structures by human microvascular endothelial cells. Moreover, ZD1839 almost completely blocked EGF-induced neovascularization of mice cornea, and SU5416 partially blocked neovascularization. In contrast, ZD1839 did not inhibit VEGF-induced angiogenesis. However, EGF-induced up-regulation of the angiogenic factors, VEGF and IL-8, was almost completely blocked by ZD1839. The antitumor effects of ZD1839 could, therefore, be mediated in part by the inhibition of tumor angiogenesis through direct effects on microvascular endothelial cells that express EGFR and also through reduced production of proangiogenic factors by tumor cells.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 30 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:331865 HCAPLUS
DOCUMENT NUMBER: 136:365750
TITLE: Diagnostic and drug screening use of cellular **kinases** involved in human cytomegalovirus infection and treatment of HCMV infection using **kinase** inhibitors
INVENTOR(S): Schubart, Daniel; Habenberger, Peter; Stein-Gerlach, Matthias; Bevec, Dorian
PATENT ASSIGNEE(S): Axxima Pharmaceuticals Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1201765	A2	20020502	EP 2001-124604	20011015
EP 1201765	A3	20030827		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003082519	A1	20030501	US 2001-981397	20011016
US 6849409	B2	20050201		
PRIORITY APPLN. INFO.:			US 2000-240750P P	20001016

AB The role of certain cellular **kinases** active during human cytomegalovirus infection is disclosed. These cellular **kinases** are useful to detect HCMV infection, and can be used to screen for cellular **kinase** inhibitors. Cellular **kinases** inhibitors, which effectively downregulate these key cellular components, serve as effective therapeutics against HCMV infection.

L15 ANSWER 31 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:275806 HCAPLUS
DOCUMENT NUMBER: 136:304047
TITLE: Effects of combined administration of farnesyl transferase inhibitors and **signal transduction** inhibitors
INVENTOR(S): Daley, George Q.; Hoover, Russell R.
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028409	A2	20020411	WO 2001-US31104	20011004
WO 2002028409	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,				

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002011427	A5	20020415	AU 2002-11427		20011004
US 2002077301	A1	20020620	US 2001-971365		20011004
US 2005020516	A1	20050127	US 2004-870403		20040617
PRIORITY APPLN. INFO.:			US 2000-238240P	P	20001005
			US 2000-238813P	P	20001006
			US 2001-971365	B1	20011004
			WO 2001-US31104	W	20011004

AB The invention relates to methods of reducing proliferation of cells, enhancing apoptosis of cells or both in an individual in need thereof, comprising administering to the individual a combination of at least one farnesyl transferase inhibitor (FTI), such as an inhibitor or Ras function, and at least one **signal transduction** inhibitor (STI) in a therapeutically effective amount, wherein proliferation of cells is reduced and/or apoptosis of cells in enhanced in the individual. The invention also discloses a method of reducing proliferation of STI resistant cells, enhancing apoptosis of STI resistant cells, or both in an individual in need thereof, comprising administering to the individual a combination of at least one FTI and at least one STI in a therapeutically effective amount, wherein proliferation of STI resistant cells is reduced and/or apoptosis of STI resistant cells is enhanced in the individual. The invention can be used to treat leukemia (e.g., CML) using this combination of farnesyl transferase inhibitor and **signal transduction** inhibitor.

L15 ANSWER 32 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:185277 HCAPLUS
DOCUMENT NUMBER: 136:242899
TITLE: Phage display libraries and methods for identifying targeting peptides in humans in vivo
INVENTOR(S): Arap, Wadih; Pasqualini, Renata
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020723	A2	20020314	WO 2001-US28044	20010907
WO 2002020723	A3	20020829		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2421195	AA	20020314	CA 2001-2421195	20010907
AU 2001090662	A5	20020322	AU 2001-90662	20010907
EP 1315830	A2	20030604	EP 2001-970681	20010907

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004533803	T2	20041111	JP 2002-525730	20010907
CA 2496938	AA	20040311	CA 2002-2496938	20021030
WO 2004020999	A1	20040311	WO 2002-US34987	20021030

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002364501	A1	20040319	AU 2002-364501	20021030
EP 1546714	A1	20050629	EP 2002-799873	20021030

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:	US 2000-231266P	P 20000908
	US 2001-765101	A 20010117
	US 2001-97651	A 20010117
	WO 2001-US28044	W 20010907
	WO 2002-US27836	A 20020830
	WO 2002-US34987	W 20021030

AB The present invention concerns methods and compns. for identifying human targeting peptides sequences. The methods used for phage display biopanning in the mouse model system require substantial improvements for use with humans. In general, humans suitable for use with phage display are either brain dead or terminal wean patients. The amount of phage library (preferably primary library) required for administration must be significantly increased, preferably 5 orders of magnitude to 1014 TU or higher, preferably administered i.v. in .apprx.200 mL of Ringer lactate solution over about a 10-min period. To produce such large phage libraries, the transformed bacterial pellets recovered from up to 500-1000 transformations are amplified up to 10 times in the bacterial host, recovering the phage from each round of amplification and adding LB Tet medium to the bacterial pellet for collection of addnl. phage. Samples of various organs and tissues are collected starting .apprx.15 min after injection of the phage library; samples are processed and phage collected from each organ, tissue or cell type of interest for DNA sequencing to determine the amino acid sequences of targeting peptides. A substantial improvement in the biopanning technique involves polyorgan targeting. It is possible to pool phage collected from multiple organs after a first round of biopanning and inject the pooled sample into a new subject, where each of the multiple organs may be collected for phage rescue, and the protocol repeated for as many rounds of biopanning as desired. In this manner, it is possible to significantly reduce the number of subjects required for isolation of targeting peptides for multiple organs, while still achieving substantial enrichment of the organ-homing phage. Thus, 320 targeting peptides are identified with specificity for bone marrow, adipose tissue, skeletal muscle, prostate, skin, or multiple organs. The peptides are of use for targeted delivery of therapeutic agents, including gene therapy vectors. Such targeted delivery may be used for detection, diagnosis or treatment of human diseases. In certain embodiments, the peptide may be attached to an imaging agent and administered to a human to obtain an image or to diagnose a disease state. Also disclosed are a large number of targeting peptide sequences and consensus motifs that are selective for human organs or tissues, obtained by the methods of the

present invention.

L15 ANSWER 33 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:917070 HCAPLUS
DOCUMENT NUMBER: 136:214530
TITLE: The t(8;22) in chronic myeloid leukemia fuses BCR to FGFR1: transforming activity and specific inhibition of FGFR1 fusion **proteins**
AUTHOR(S): Demiroglu, Asuman; Steer, E. Joanna; Heath, Carol; Taylor, Kerry; Bentley, Mark; Allen, Steven L.; Koduru, Prasad; Brody, Judith P.; Hawson, Geoffrey; Rodwell, Robyn; Doody, Mary-Lou; Carnicero, Fernando; Reiter, Andreas; Goldman, John M.; Melo, Junia V.; Cross, Nicholas C. P.
CORPORATE SOURCE: Department of Haematology, Imperial College School of Medicine, Hammersmith Hospital, London, UK
SOURCE: Blood (2001), 98(13), 3778-3783
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This report describes 2 patients with a clin. and hematol. diagnosis of chronic myeloid leukemia (CML) in chronic phase who had an acquired t(8;22)(p11;q11). Anal. by fluorescence in situ hybridization (FISH) and reverse transcription-polymerase chain reaction (RT-PCR) indicated that both patients were neg. for the BCR-ABL fusion, but suggested that the BCR gene was disrupted. Further FISH indicated a breakpoint within fibroblast growth factor receptor 1 (FGFR1), the receptor tyrosine **kinase** that is known to be disrupted in a distinctive myeloproliferative disorder, most commonly by fusion to ZNF198. RT-PCR confirmed the presence in both cases of an in-frame mRNA fusion between BCR exon 4 and FGFR1 exon 9. Expression of BCR-FGFR1 in the factor-dependent cell line Ba/F3 resulted in interleukin 3-independent clones that grew at a comparable rate to cells transformed with ZNF198-FGFR1. The growth of transformed cells was inhibited by the phosphatidylinositol 3-**kinase** inhibitor LY294002, the farnesyltransferase inhibitors L744832 and manumycin A, the p38 inhibitors SB202190 and SB203580 but not by the MEK inhibitor PD98059. The growth of BaF3/BCR-FGFR1 and BaF3/ZNF198-FGFR1 was not significantly inhibited by treatment with STI571, but was inhibited by SU5402, a compound with inhibitory activity against FGFR1. Inhibition with this compound was associated with decreased phosphorylation of ERK1/2 and BCR-FGFR1 or ZNF198-FGFR1, and was dose dependent with an inhibitory concentration of 50% of approx. 5 μM. As expected, growth of BaF3/BCR-ABL was inhibited by STI571 but not by SU5402. The study demonstrates that the BCR-FGFR1 fusion may occur in patients with apparently typical CML. Patients with constitutively active FGFR1 fusion genes may be amenable to treatment with specific FGFR1 inhibitors.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 34 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:472477 HCAPLUS
DOCUMENT NUMBER: 135:56059
TITLE: Methods of modulating c-kit tyrosine **protein kinase** function with indolinone compounds
INVENTOR(S): Lipson, Ken; McMahon, Gerald
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001045689	A2	20010628	WO 2000-US35009		20001222
WO 2001045689	A3	20020103			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2395461	AA	20010628	CA 2000-2395461		20001222
US 2002010203	A1	20020124	US 2000-741842		20001222
EP 1255536	A2	20021113	EP 2000-991704		20001222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004500363	T2	20040108	JP 2001-546428		20001222
NZ 519697	A	20040827	NZ 2000-519697		20001222
US 2004002534	A1	20040101	US 2003-600868		20030623
US 2005288353	A1	20051229	US 2005-205474		20050816
PRIORITY APPLN. INFO.:			US 1999-171693P	P	19991222
			US 2000-741842	B1	20001222
			WO 2000-US35009	W	20001222
			US 2003-600868	A1	20030623

OTHER SOURCE(S): MARPAT 135:56059

AB The invention concerns indolinone compds. and their use to inhibit the activity of a receptor tyrosine **kinase.** The invention is preferably used to treat cell proliferative disorders such as cancers characterized by over-activity or inappropriate activity of c-kit **kinase.**

L15 ANSWER 35 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:688215 HCAPLUS
DOCUMENT NUMBER: 133:252306
TITLE: Preparation of indolinones as **protein kinase** inhibitors.
INVENTOR(S): Tang, Peng Cho; Sun, Li; Mcmahon, Gerald; Miller, Todd Anthony; Shirazian, Shahrzad; Wei, Chung Chen; Harris, G. Davis; Xiaoyuan, Li; Liang, Congxin
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 245 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056709	A1	20000928	WO 2000-US7704	20000322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,				

CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
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LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
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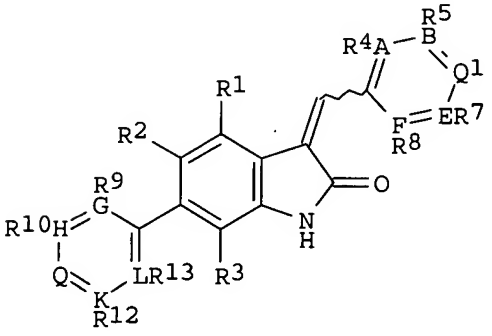
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2368041	AA	20000928	CA 2000-2368041		20000322
EP 1165513	A1	20020102	EP 2000-916622		20000322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002540096	T2	20021126	JP 2000-606571		20000322
US 6689806	B1	20040210	US 2000-534405		20000322
PRIORITY APPLN. INFO.:			US 1999-125945P	P	19990324
			US 1999-127863P	P	19990405
			US 1999-131192P	P	19990426
			US 1999-132243P	P	19990503
			WO 2000-US7704	W	20000322

OTHER SOURCE(S): MARPAT 133:252306
GI



I

AB Title compds., e.g. [I; m, n = 0, 1; Q = (JR11)m; Q1 = (DR6)n; when n = 1, then A, B, D, E, F = C, N; ≤3 of A, B, D, E, F = N; when m = 1, then G, H, J, K, L = C, N; ≥1 and ≤3 of G, H, J, K, L = N; when n = 0, then A = C, N, B, F = C, N, NH, O, S; E = C, N, O, S; when m = O, then G = C, N, H, K, 1 = C, N, NH, O, S; R1-R13 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, SH, alkylthiol, aryloxy, amino, etc.; R4R5 or R5R6 or R6R7 or R7R8 = atoms to form a 5-6 membered (hetero)aryl ring; with addnl. provisos], were prepared Thus, 6-pyridin-3-yl-1,3-dihydroindol-2-one (preparation given), 4-methoxy-3-thien-2-ylbenzaldehyde, and piperidine were refluxed overnight in EtOH to give 15% 3-(4-methoxy-3-thien-2-ylbenzylidene)-6-pyridin-3-yl-1,3-dihydroindol-2-one. Tested title compds. inhibited HER2 **kinase** with IC50 = 16.4 μM to ≥100 μM.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 36 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:509842 HCAPLUS
DOCUMENT NUMBER: 133:348326

TITLE: Targeting angiogenesis inhibits tumor infiltration and expression of the pro-invasive **protein** SPARC
AUTHOR(S): Vajkoczy, Peter; Menger, Michael D.; Goldbrunner, Roland; Ge, Shugang; Annie, T.; Fong, T.; Vollmar, Brigitte; Schilling, Lothar; Ullrich, Axel; Hirth, K. Peter; Tonn, Jorg C.; Schmiedek, Peter; Rempel, Sandra A.
CORPORATE SOURCE: Department of Neurosurgery. Klinikum Mannheim, University of Heidelberg, Mannheim, D-68167, Germany
SOURCE: International Journal of Cancer (2000), 87(2), 261-268
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The solid growth of high-grade glioma appears to be critically dependent on tumor angiogenesis. It remains unknown, however, whether the diffuse infiltration of glioma cells into healthy adjacent tissue is also dependent on the formation of new tumor vessels. Here, the authors analyze the relation between tumor angiogenesis and tumor cell infiltration in an exptl. glioma model. C6 cells were implanted into the dorsal skinfold chamber of nude mice, and tumor angiogenesis was monitored by intravital fluorescence videomicroscopy. Glioma infiltration was assessed by the extent of tumor cell invasion into the adjacent chamber tissue and by expression of SPARC, a cellular marker of glioma invasiveness. To test the hypothesis that glioma angiogenesis and glioma infiltration are codependent, the authors assessed tumor infiltration in both the presence and the absence of the angiogenesis inhibitor SU5416. SU5416 is a selective inhibitor of the VEGF/Flk-I **signal-transduction** pathway, a critical pathway implicated in angiogenesis. Control tumors demonstrated both high angiogenic activity and tumor cell invasion accompanied by strong expression of SPARC in invading tumor cells at the tumor-host tissue border. SU5416-treated tumors demonstrated reduced vascular d. and vascular surface in the tumor periphery accompanied by marked inhibition of glioma invasion and decreased SPARC expression. A direct effect of SU5416 on glioma cell motility and invasiveness was excluded by in vitro migration and invasion assays. These results suggest a crucial role for glioma-induced angiogenesis as a prerequisite for diffuse tumor invasion and a possible therapeutic role for anti-angiogenic compds. as inhibitors of both solid and diffuse infiltrative tumor growth.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 37 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:626172 HCAPLUS
DOCUMENT NUMBER: 131:257441
TITLE: Heterocyclic families of compounds [tricyclic-based indolinones and pyrazolecarboxylic acid amides] for the modulation of tyrosine **protein kinase**
INVENTOR(S): Fong, Annie; Hannah, Alison; Harris, David G.; Hirth, Peter; Hubbard, Steven R.; Langecker, Peter; Liang, Congxin; McMahon, Gerald; Mohammadi, Moosa; Schlessinger, Joseph; Shawver, Laura K.; Sun, Li; Tang, Peng C.; Ullrich, Axel
PATENT ASSIGNEE(S): Sugen, Inc., USA; New York University; Max-Planck Institut fur Biochemie
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948868	A2	19990930	WO 1999-US6468	19990326
WO 9948868	A3	20000224		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2325935	AA	19990930	CA 1999-2325935	19990326
AU 9933635	A1	19991018	AU 1999-33635	19990326
EP 1066257	A2	20010110	EP 1999-915018	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002507598	T2	20020312	JP 2000-537851	19990326
US 6514981	B1	20030204	US 1999-283657	19990401
US 2003203901	A1	20031030	US 2002-302932	20021125

PRIORITY APPLN. INFO.:	US 1998-79713P	P	19980326
	US 1998-80422P	P	19980402
	US 1998-81792P	P	19980415
	US 1998-82056P	P	19980416
	US 1998-89397P	P	19980615
	US 1998-89521P	P	19980616
	US 1998-98783P	P	19980901
	WO 1999-US6468	W	19990326
	US 1999-283657	A3	19990401

OTHER SOURCE(S): MARPAT 131:257441
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to certain indolinone-based and pyrazolylamide-based compds., I and II, their method of synthesis, and combinatorial libraries consisting of the compds. [wherein AB = atoms to make up 1-2 fused and/or connected rings; R = aromatic or heteroarom. ring which may form an addnl. ring by cyclization to the methylene group; R1, R2 = H, alkyl, (hetero)aryl or -aliphatic ring, amino, NO2, halo, etc.; R3 = (un)substituted Ph; Z = (un)substituted (CH2)0-3; R4, R5 = H, alkyl, (hetero)aryl or -aliphatic, amine, ketone, etc.]. The invention also relates to methods of modulating the function of **protein kinases** using these compds., and methods of treating diseases by modulating the function of **protein kinases** and related **signal transduction** pathways. Data for prepns. and/or biol. activity are given, as well as the prepns. of various oxindole intermediates. For instance, the pyrazolecarboxamide derivative III gave up to 70% inhibition of growth of Calu-6 human lung carcinoma cells as a xenograft in mice. As another example, the indolinone derivative IV was prepared by condensation of 6-(4-methoxyphenyl)-2-oxindole with 3,5-dimethyl-1H-pyrrole-2-

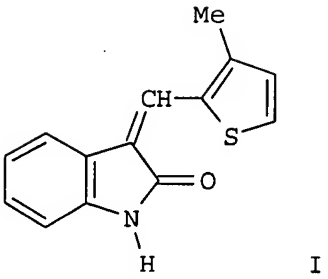
carboxaldehyde in the presence of piperidine. Extensive tests of a few selected compds. against a variety of **protein kinases** are described.

L15 ANSWER 38 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:193848 HCAPLUS
DOCUMENT NUMBER: 130:237471
TITLE: 3-(2-Alkoxybenzylidene)-2-indolinones and their analogs for the treatment of disease
INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 485,323.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5883116	A	19990316	US 1996-655224	19960605
US 5880141	A	19990309	US 1995-485323	19950607
CA 2192797	AA	19961219	CA 1996-2192797	19960605
JP 10504323	T2	19980428	JP 1997-501363	19960605
JP 3231044	B2	20011119		
EP 934931	A2	19990811	EP 1999-103667	19960605
EP 934931	A3	19991020		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 2000026412	A2	20000125	JP 1999-159567	19960605
ES 2159741	T3	20011016	ES 1996-918093	19960605
PT 769947	T	20011031	PT 1996-918093	19960605
US 6846839	B1	20050125	US 1999-333703	19990616
US 2002102608	A1	20020801	US 2001-897755	20010703
US 6906093	B2	20050614		

PRIORITY APPLN. INFO.:	US 1995-485323	A2 19950607
	EP 1996-918093	A3 19960605
	JP 1997-501363	A3 19960605
	US 1996-655223	A2 19960605
	US 1996-655224	A2 19960605
	US 1996-655226	A2 19960605
	US 1996-655255	B2 19960605
	US 1996-659191	A2 19960605
	US 1996-702232	B2 19960823
	US 1997-915366	A2 19970820

OTHER SOURCE(S): MARPAT 130:237471
GI



I

AB Indolinones such as I were prepared for modulating tyrosine **kinase signal transduction** in order to regulate, modulate, and/or inhibit abnormal cell proliferation. Thus, a mixture of 134.0 mg oxindole, 151.4 mg 3-methyl-2-thiophenecarboxaldehyde, and 3 drops of piperidine in 2 mL EtOH was stirred at 90° for 3 h to give a 65% yield of I. In an ELISA assay to measure the inhibition of **protein** tyrosine **kinase** activity on the FLK-1 receptor, I showed an IC50 of 4.5 μM.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

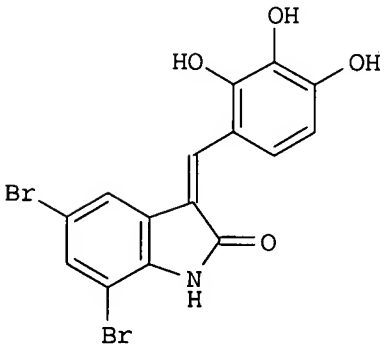
L15 ANSWER 39 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:147306 HCAPLUS
DOCUMENT NUMBER: 128:204803
TITLE: Indolinone combinatorial libraries and related products and methods for the treatment of disease
INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald; Hirth, Klaus Peter; Shawver, Laura Kay; et al.
PATENT ASSIGNEE(S): Sugen, Inc., USA; Tang, Peng Cho; Sun, Li; McMahon, Gerald
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807695	A1	19980226	WO 1997-US14736	19970820
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CN 1155838	A	19970730	CN 1996-190616	19960605
CA 2264220	AA	19980226	CA 1997-2264220	19970820
EP 929520	A1	19990721	EP 1997-939480	19970820
EP 929520	B1	20051102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001503736	T2	20010321	JP 1998-510973	19970820

EP 1247803	A2	20021009	EP 2002-77564		19970820
EP 1247803	A3	20021016			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 308520	E	20051115	AT 1997-939480		19970820
AU 9741556	A1	19980306	AU 1997-41556		19970821
PRIORITY APPLN. INFO.:			US 1996-702232	A	19960823
			US 1996-31585P	P	19961205
			US 1996-31586P	P	19961205
			US 1996-31588P	P	19961205
			US 1996-32546P	P	19961205
			US 1996-32547P	P	19961205
			US 1997-45565P	P	19970505
			US 1997-45566P	P	19970505
			US 1997-45714P	P	19970505
			US 1997-45715P	P	19970505
			US 1997-46843P	P	19970505
			EP 1997-939480	A3	19970820
			WO 1997-US14736	W	19970820

OTHER SOURCE(S): MARPAT 128:204803

GI



I

AB The invention relates to indolinone derivs. capable of modulating, regulating, and/or inhibiting **protein kinase signal transduction.** The compds. are useful for the treatment of diseases related to unregulated **protein kinase signal transduction**, including cell proliferative diseases such as cancer, atherosclerosis, arthritis, and restenosis, and metabolic diseases such as diabetes. Inhibitors specific to the FLK **protein kinase** can be obtained by adding chemical substituents to the 3-[(indole-3-yl)methylene]-2-indolinone system, in particular at the 1' position of the indole ring. Indolinone compds. that specifically inhibit the FLK and platelet derived growth factor **protein kinases** can harbor a tetrahydroindole or cyclopentano[b]pyrrole moiety. Indolinone compds. that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate **protein kinases.** This invention also features novel hydrosol. indolinone compds. that are tyrosine **kinase** inhibitors, and related products and methods. Approx. 1200 title compds., such as I, were prepared by combinatorial condensation of certain (un)substituted indolinones with aldehydes at the 3-position. I

gave complete inhibition of MET **kinase** at chimeric MET receptors in vitro.

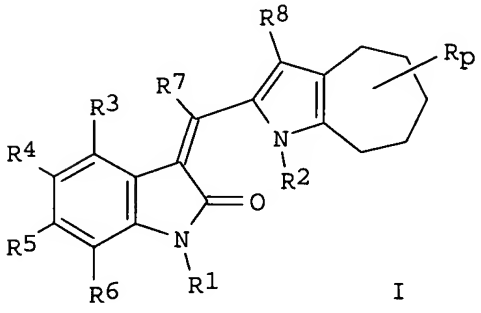
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l4 ibib abs hitstr tot

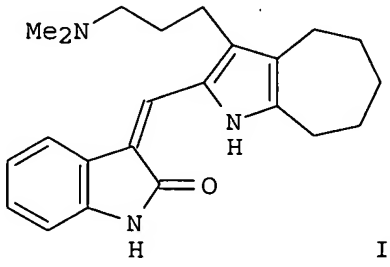
L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:780367 HCAPLUS
DOCUMENT NUMBER: 141:295860
TITLE: Preparation of hexahydro-cyclohepta[b]pyrrole oxindole as potent kinase inhibitors
INVENTOR(S): Tang, Peng Cho; Xia, Yi; Hawtin, Rachael
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004186160	A1	20040923	US 2003-733803		20031212
PRIORITY APPLN. INFO.:			US 2002-433022P	P	20021213

OTHER SOURCE(S): MARPAT 141:295860
GI



I



II

AB Indolinone compds., hexahydro-cyclohepta[b]pyrrole oxindoles of formula I [R1, R2 = H, alkyl, cycloalkyl, aryl, etc.; R3-R6 = H, halo, alkyl, cycloalkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.; R7 = H, alkyl, cycloalkyl, aryl, OH, CN, etc.; R8 = H, alkyl, cycloalkyl, aryl, hydroxyalkylene, etc.; R9 = H, alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl; p = 1-2], are prepared which are useful as protein kinase inhibitors. Thus, II was prepared from 3-(3-dimethylaminopropyl)-1,4,5,6,7,8-hexahydro-cyclohepta[b]pyrrole-2-carbaldehyde (preparation given) and 2-oxindole.

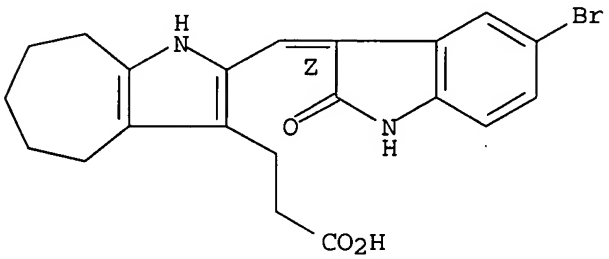
IT **760997-72-6P 760997-73-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of hexahydro-cycloheptapyrrole oxindole as protein kinase inhibitors)

RN 760997-72-6 HCAPLUS

CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

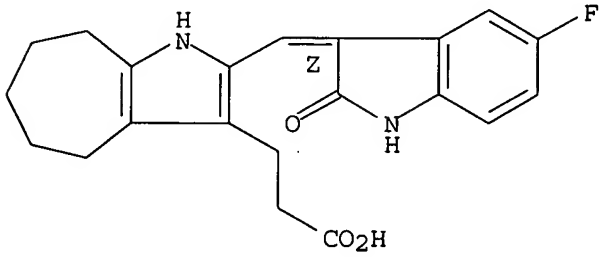
Double bond geometry as shown.



RN 760997-73-7 HCAPLUS

CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **760997-43-1P 760997-44-2P 760997-45-3P**
760997-46-4P 760997-47-5P 760997-48-6P
760997-49-7P 760997-50-0P 760997-51-1P
760997-52-2P 760997-53-3P 760997-54-4P
760997-55-5P 760997-56-6P 760997-57-7P
760997-58-8P 760997-59-9P 760997-60-2P
760997-61-3P 760997-62-4P 760997-63-5P
760997-64-6P 760997-65-7P 760997-66-8P
760997-67-9P 760997-68-0P 760997-69-1P
760997-70-4P 760997-71-5P 760997-74-8P
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760997-84-0P 760997-85-1P 760997-86-2P
760997-87-3P 760997-88-4P 760997-89-5P
760997-90-8P 760997-91-9P 760997-92-0P
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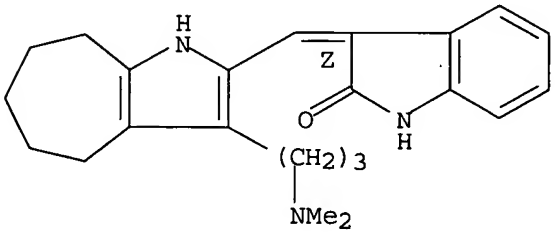
760998-05-8P 760998-06-9P 760998-07-0P
760998-08-1P 760998-09-2P 760998-10-5P
760998-11-6P 760998-12-7P 760998-13-8P

760998-14-9P 760998-15-0P 760998-16-1P
760998-17-2P 760998-18-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hexahydro-cycloheptapyrrole oxindole as protein kinase inhibitors)

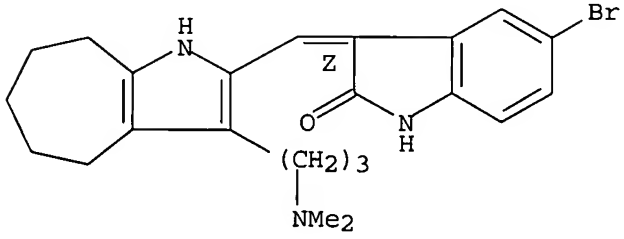
RN 760997-43-1 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



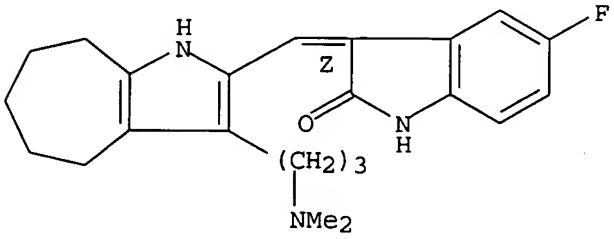
RN 760997-44-2 HCAPLUS
CN 2H-Indol-2-one, 5-bromo-3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 760997-45-3 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

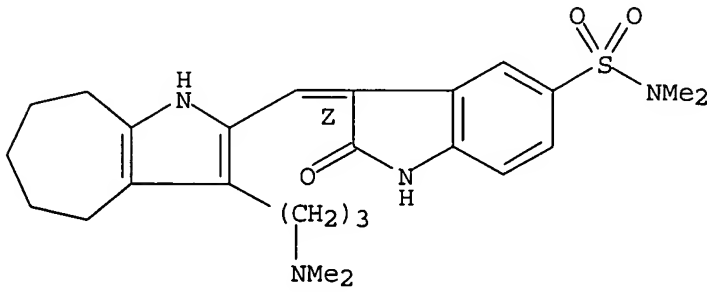
Double bond geometry as shown.



RN 760997-46-4 HCAPLUS

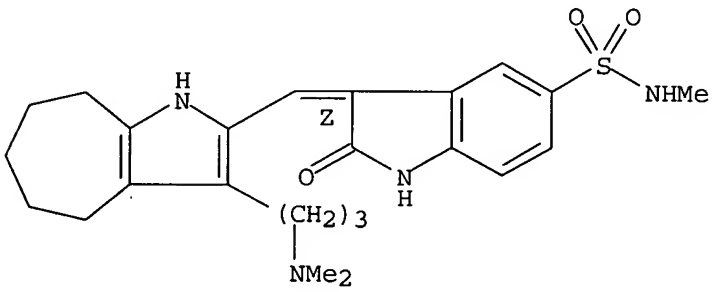
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



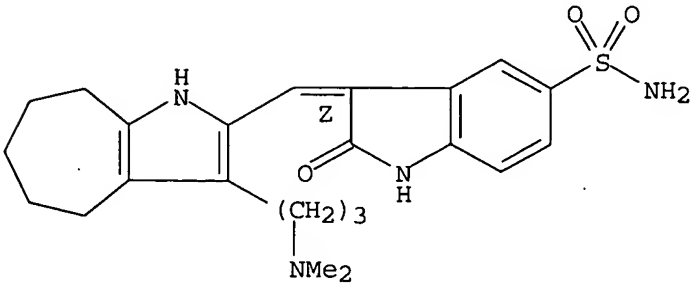
RN 760997-47-5 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 760997-48-6 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

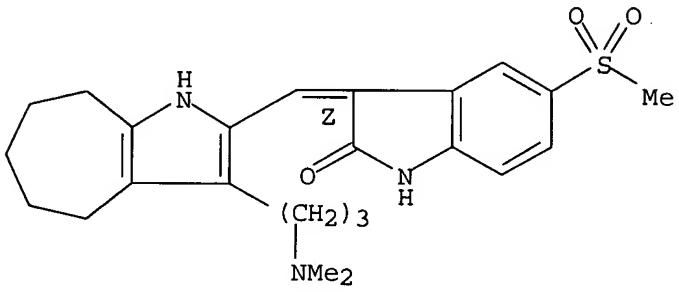
Double bond geometry as shown.



RN 760997-49-7 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-

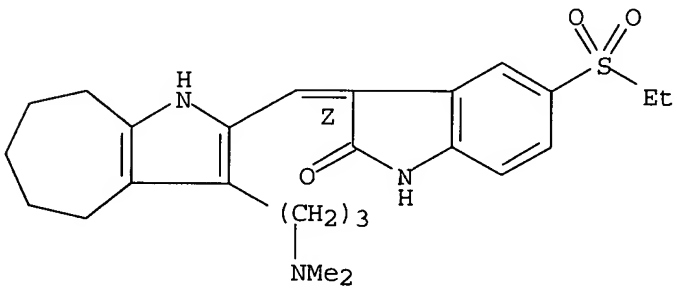
(methylsulfonyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



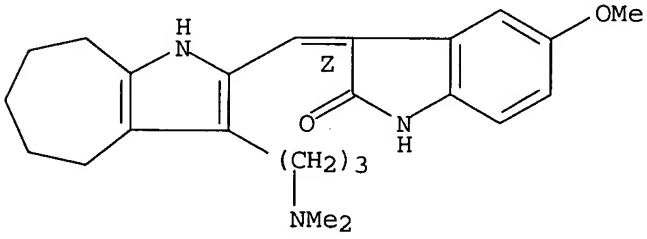
RN 760997-50-0 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-5-(ethylsulfonyl)-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



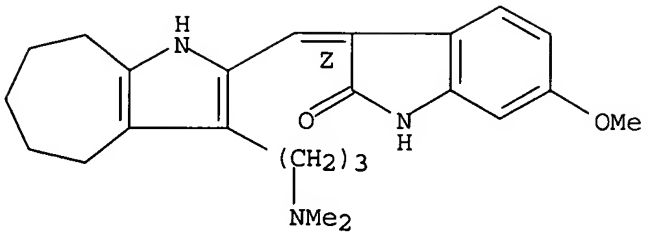
RN 760997-51-1 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-methoxy-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



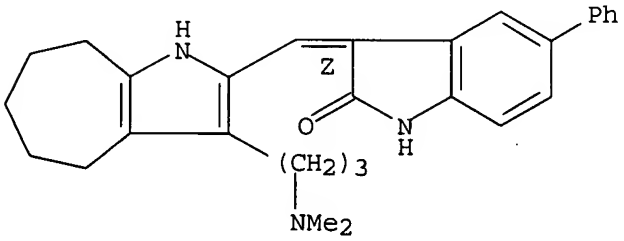
RN 760997-52-2 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-6-methoxy-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



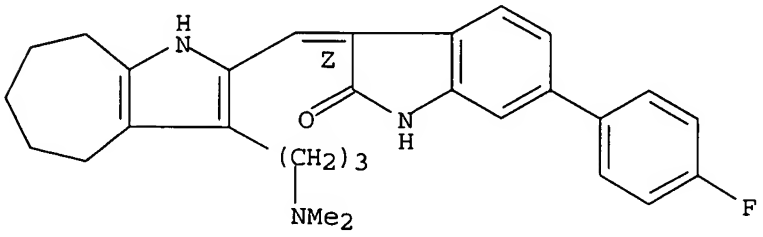
RN 760997-53-3 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-phenyl-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



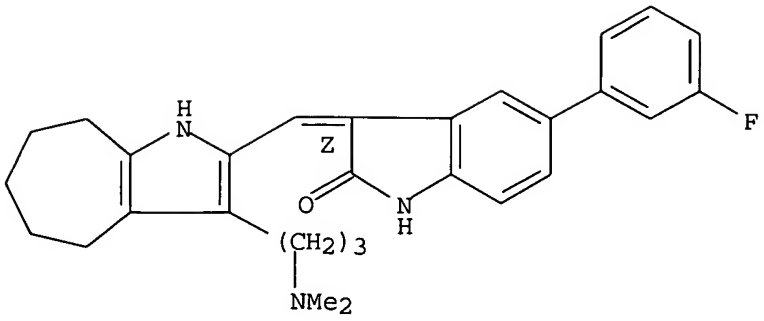
RN 760997-54-4 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-6-(4-fluorophenyl)-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



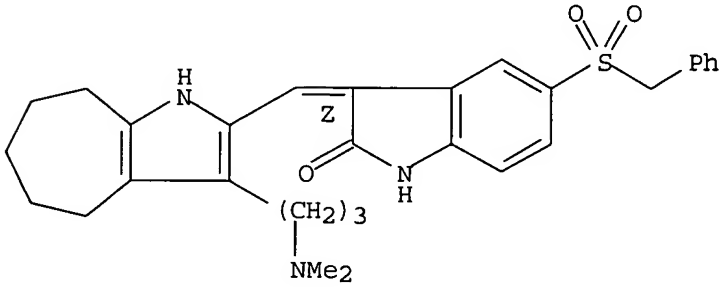
RN 760997-55-5 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-5-(3-fluorophenyl)-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



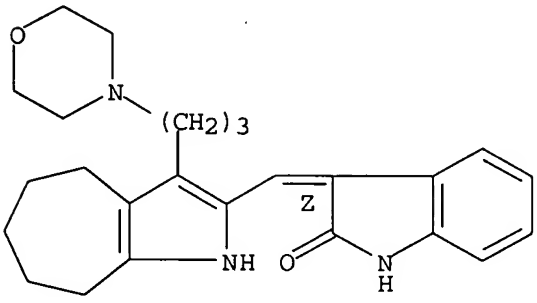
RN 760997-56-6 HCAPLUS
CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-[(phenylmethyl)sulfonyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



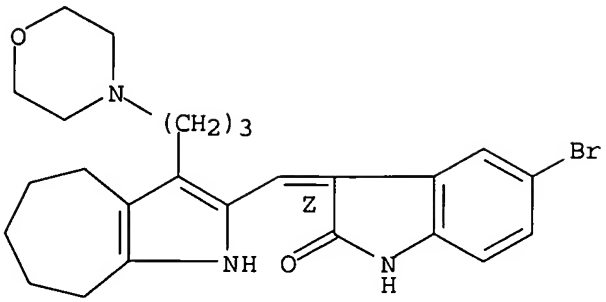
RN 760997-57-7 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



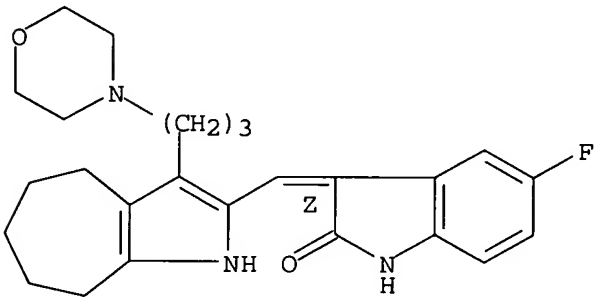
RN 760997-58-8 HCAPLUS
CN 2H-Indol-2-one, 5-bromo-3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



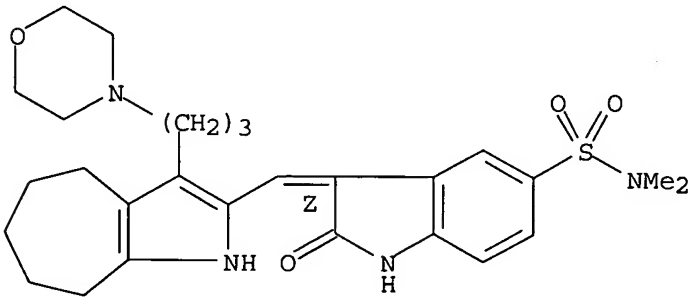
RN 760997-59-9 HCAPLUS
CN 2H-Indol-2-one, 5-fluoro-3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



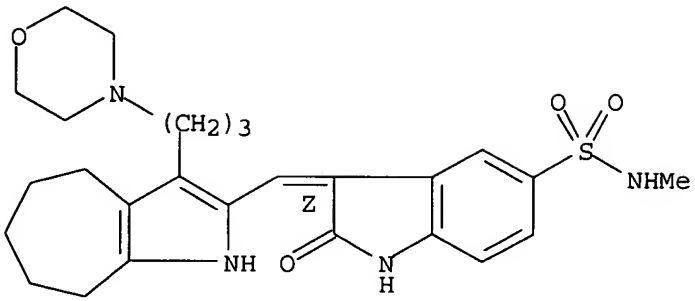
RN 760997-60-2 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



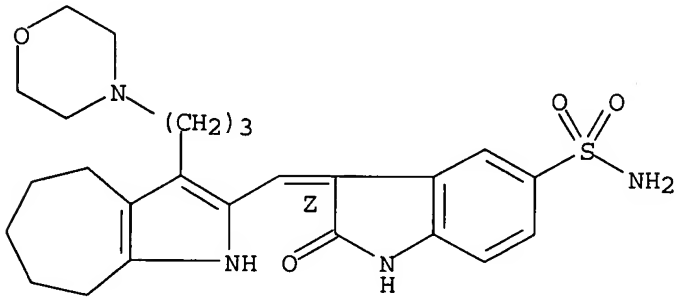
RN 760997-61-3 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



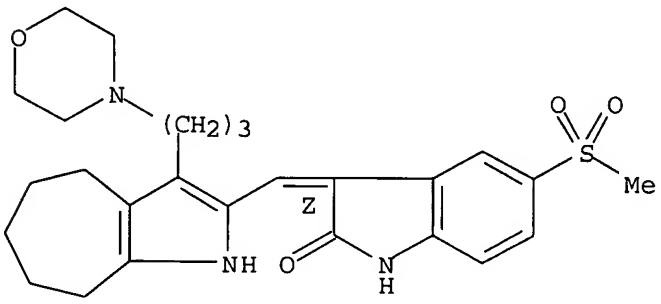
RN 760997-62-4 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



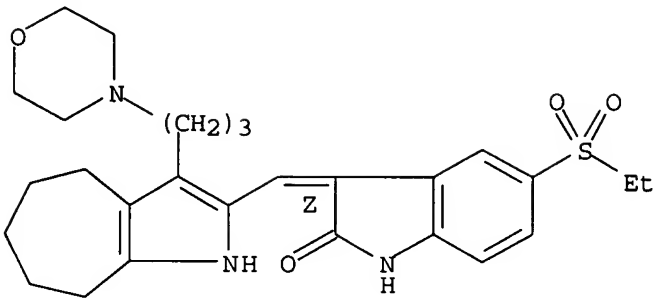
RN 760997-63-5 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-(methylsulfonyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



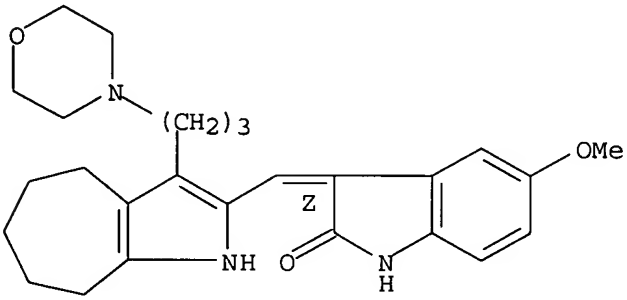
RN 760997-64-6 HCAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



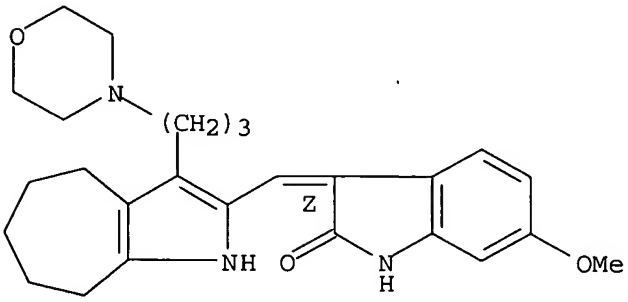
RN 760997-65-7 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-methoxy-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



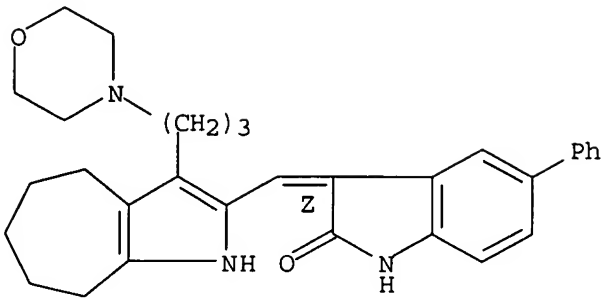
RN 760997-66-8 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-6-methoxy-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



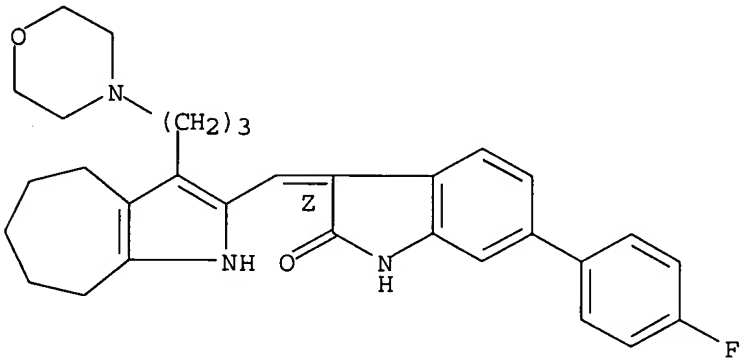
RN 760997-67-9 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-phenyl-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



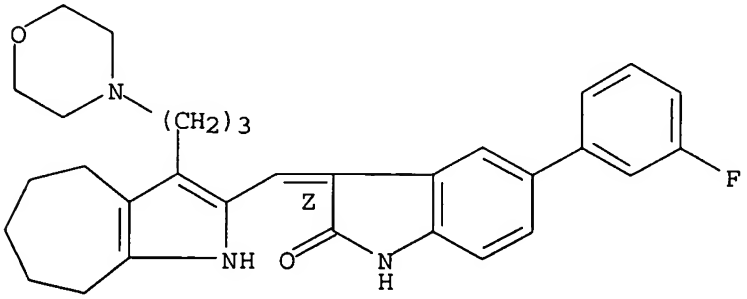
RN 760997-68-0 HCAPLUS
CN 2H-Indol-2-one, 6-(4-fluorophenyl)-3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



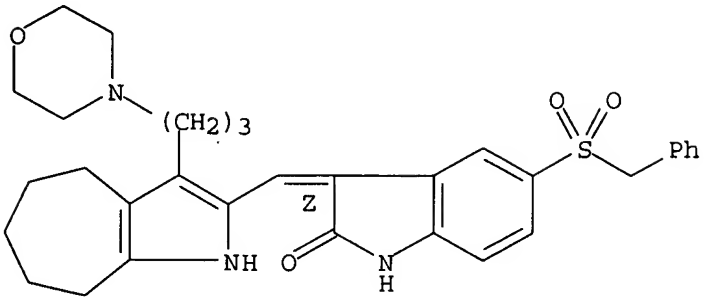
RN 760997-69-1 HCAPLUS
CN 2H-Indol-2-one, 5-(3-fluorophenyl)-3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



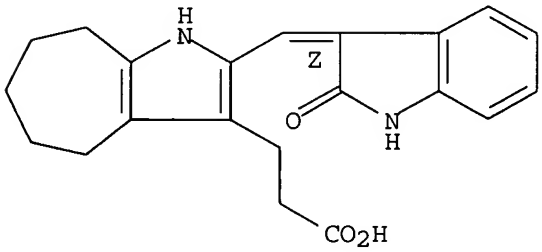
RN 760997-70-4 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-[3-(4-morpholinyl)propyl]cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-[(phenylmethyl)sulfonyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



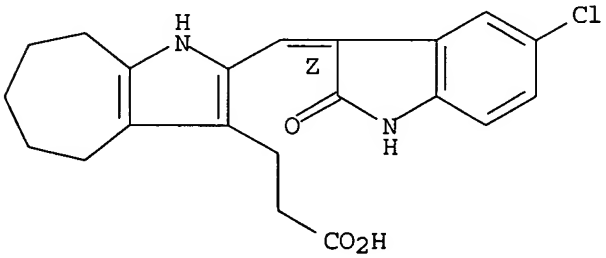
RN 760997-71-5 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



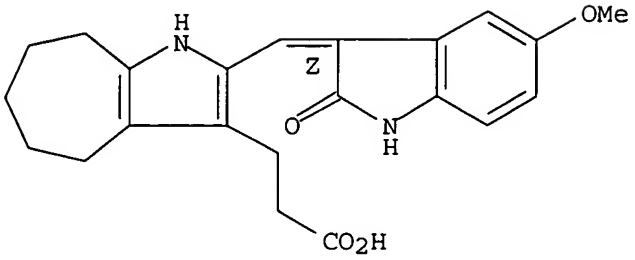
RN 760997-74-8 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



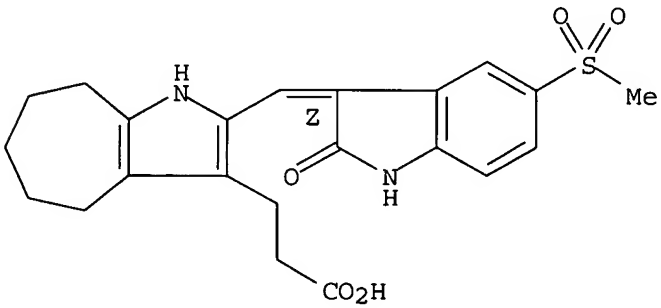
RN 760997-75-9 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



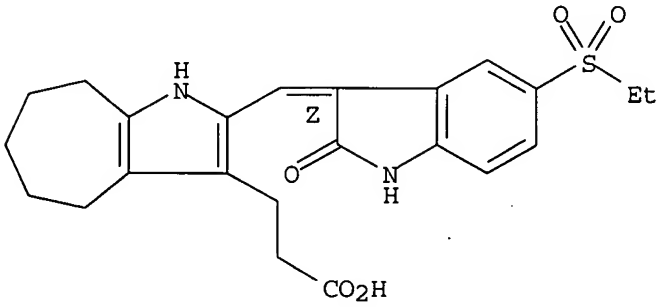
RN 760997-76-0 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-5-(methylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



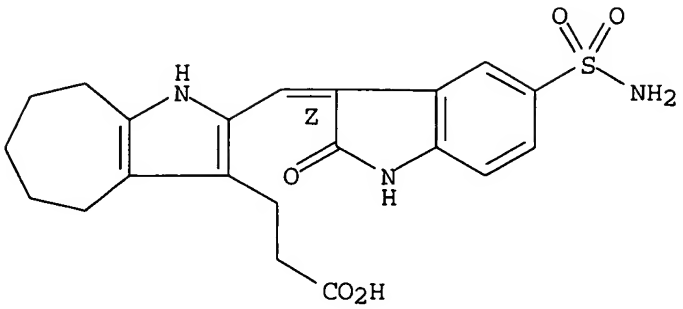
RN 760997-77-1 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[5-(ethylsulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



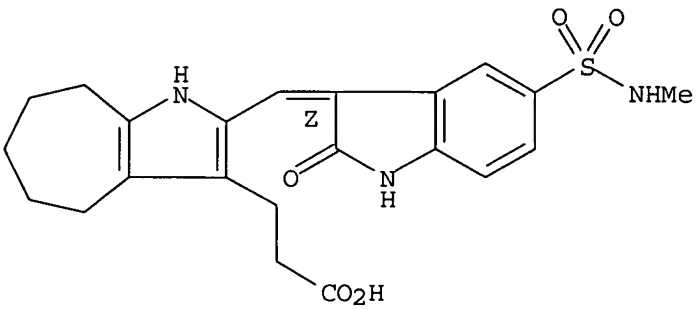
RN 760997-78-2 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



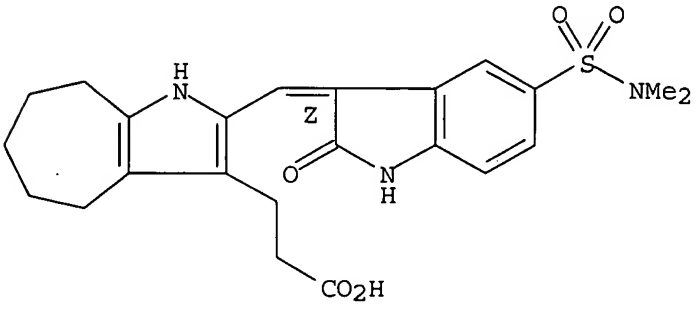
RN 760997-79-3 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



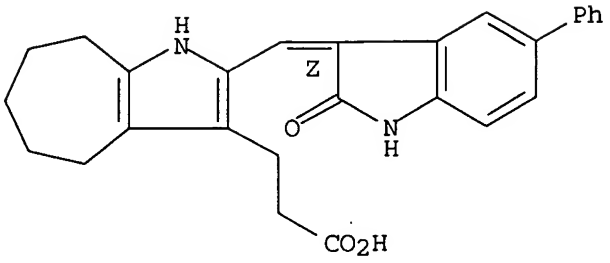
RN 760997-80-6 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[5-[(dimethylamino)sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



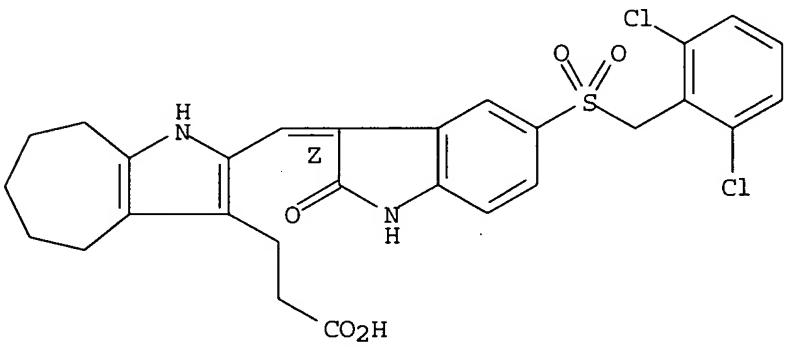
RN 760997-81-7 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



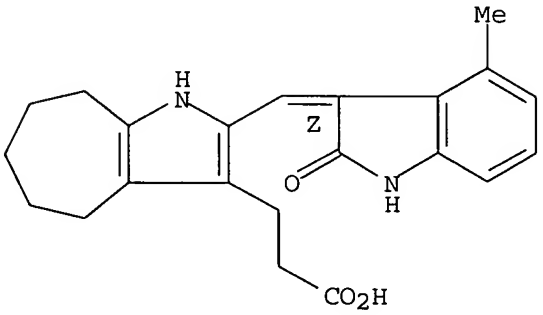
RN 760997-82-8 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[5-[[(2,6-dichlorophenyl)methyl]sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



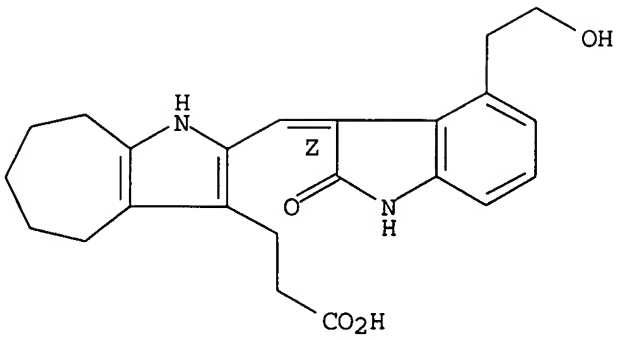
RN 760997-83-9 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



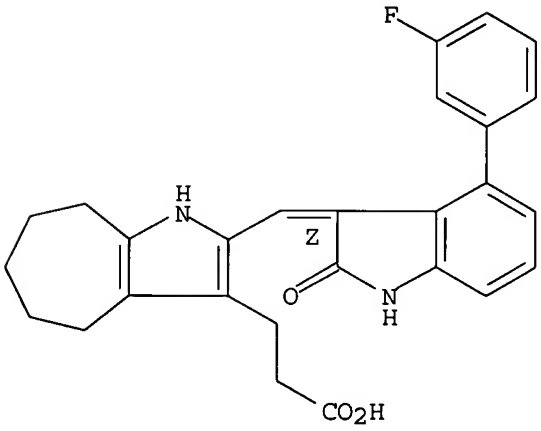
RN 760997-84-0 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-4-(2-hydroxyethyl)-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



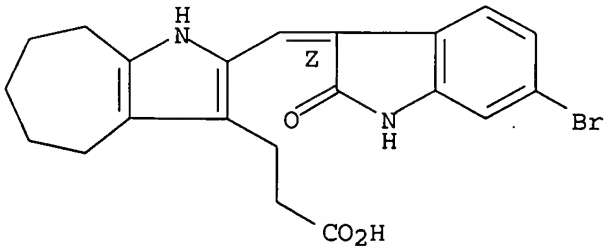
RN 760997-85-1 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-[4-(3-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



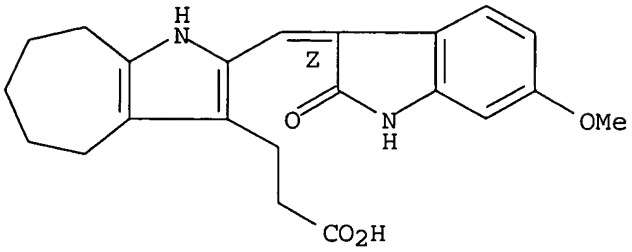
RN 760997-86-2 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(6-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



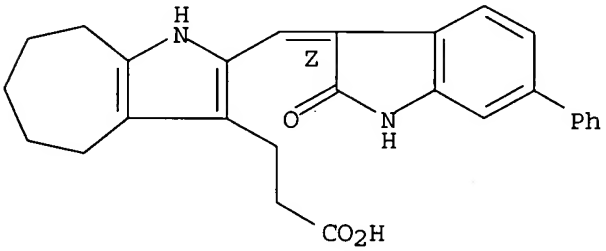
RN 760997-87-3 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



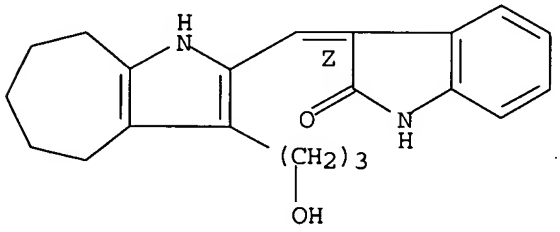
RN 760997-88-4 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



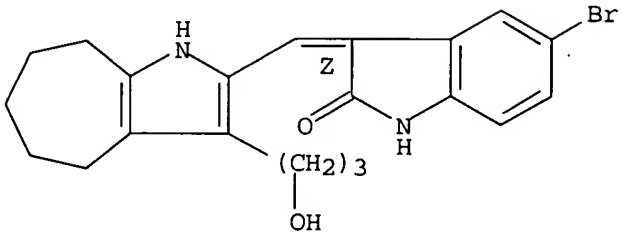
RN 760997-89-5 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



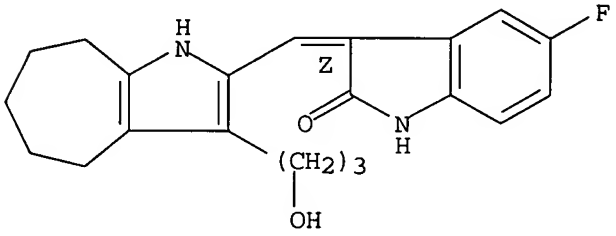
RN 760997-90-8 HCAPLUS
CN 2H-Indol-2-one, 5-bromo-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



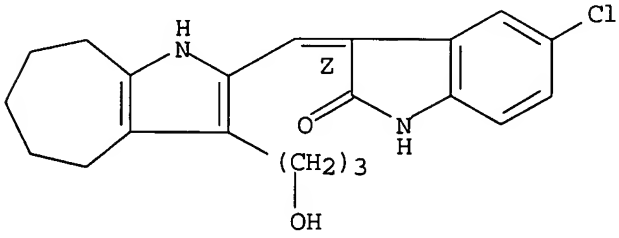
RN 760997-91-9 HCAPLUS
CN 2H-Indol-2-one, 5-fluoro-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



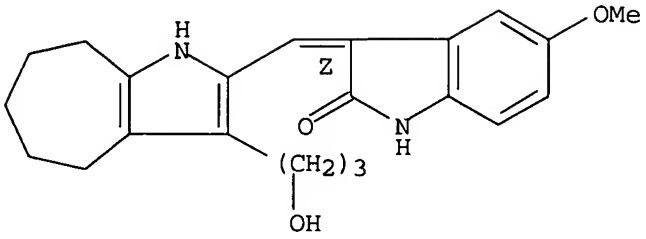
RN 760997-92-0 HCAPLUS
CN 2H-Indol-2-one, 5-chloro-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



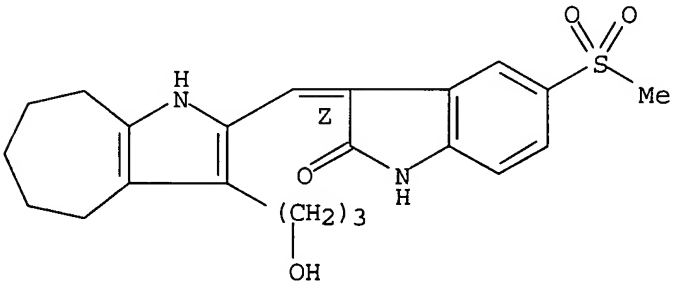
RN 760997-93-1 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-methoxy-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



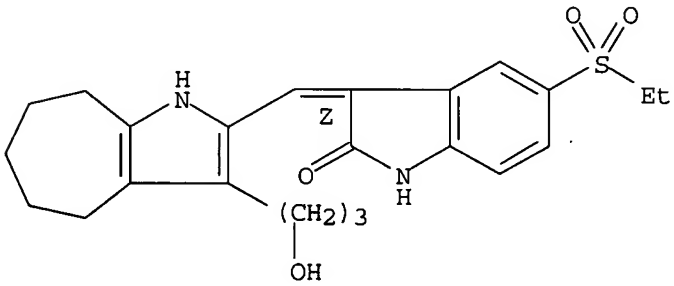
RN 760997-94-2 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-(methylsulfonyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



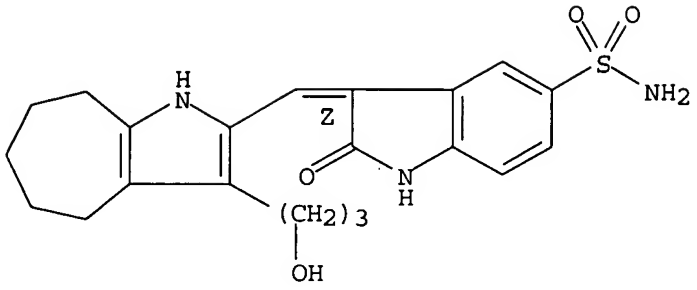
RN 760997-95-3 HCAPLUS
CN 2H-Indol-2-one, 5-(ethylsulfonyl)-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



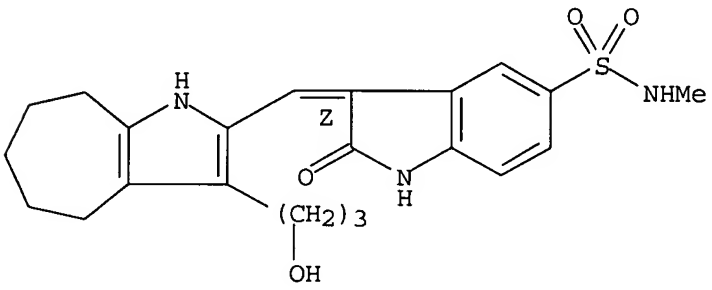
RN 760997-96-4 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



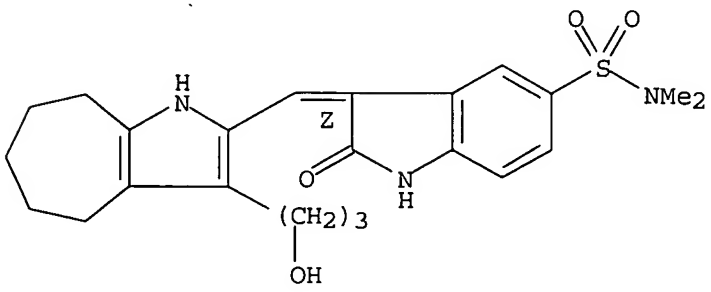
RN 760997-97-5 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



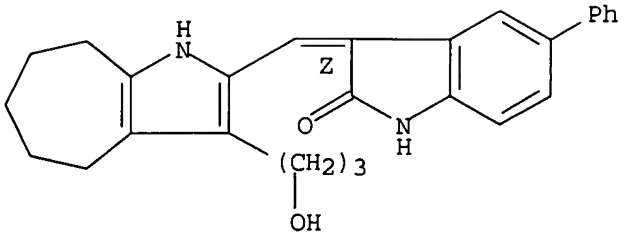
RN 760997-98-6 HCAPLUS
CN 1H-Indole-5-sulfonamide, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



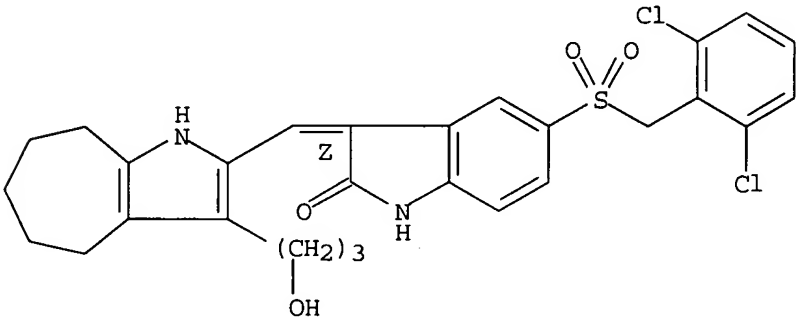
RN 760997-99-7 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-5-phenyl-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



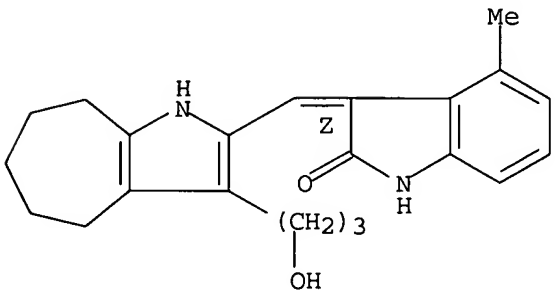
RN 760998-00-3 HCAPLUS
CN 2H-Indol-2-one, 5-[[(2,6-dichlorophenyl)methyl]sulfonyl]-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



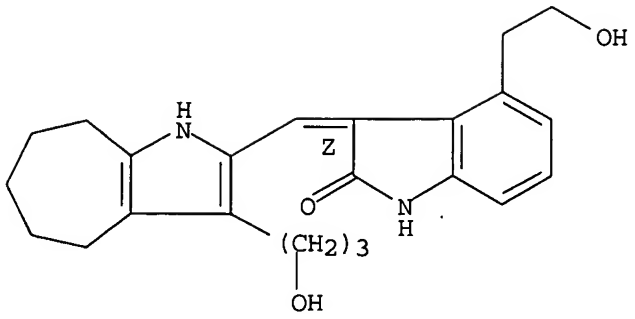
RN 760998-01-4 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-4-methyl-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



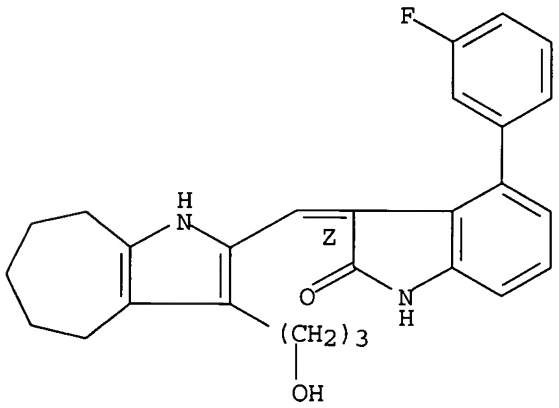
RN 760998-02-5 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-4-(2-hydroxyethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



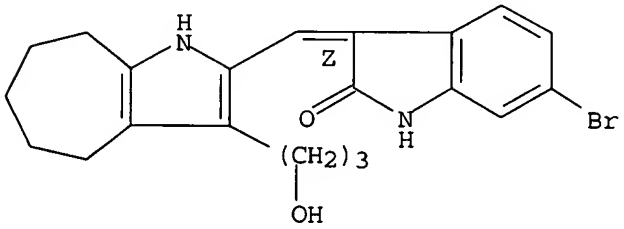
RN 760998-03-6 HCAPLUS
CN 2H-Indol-2-one, 4-(3-fluorophenyl)-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



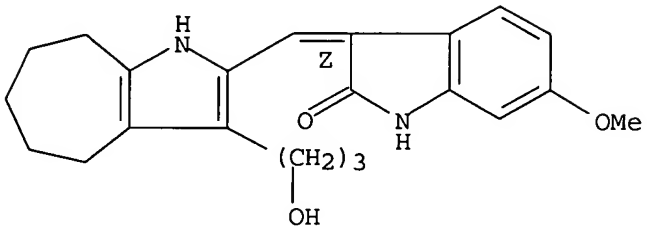
RN 760998-04-7 HCAPLUS
CN 2H-Indol-2-one, 6-bromo-3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



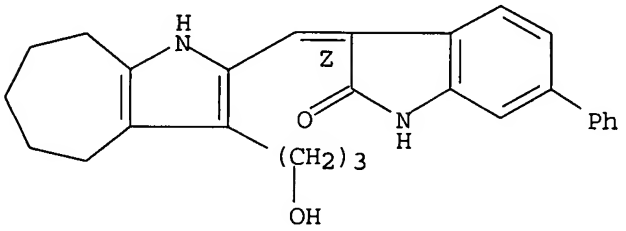
RN 760998-05-8 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-6-methoxy-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



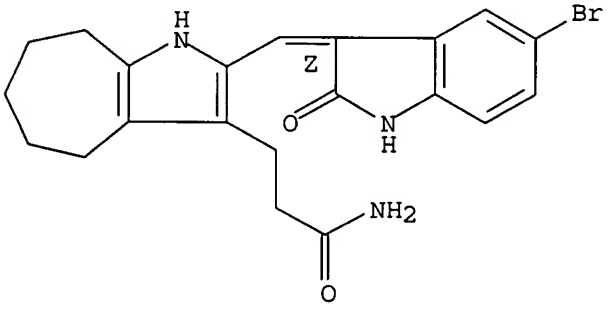
RN 760998-06-9 HCAPLUS
CN 2H-Indol-2-one, 3-[[1,4,5,6,7,8-hexahydro-3-(3-hydroxypropyl)cyclohepta[b]pyrrol-2-yl]methylene]-1,3-dihydro-6-phenyl-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



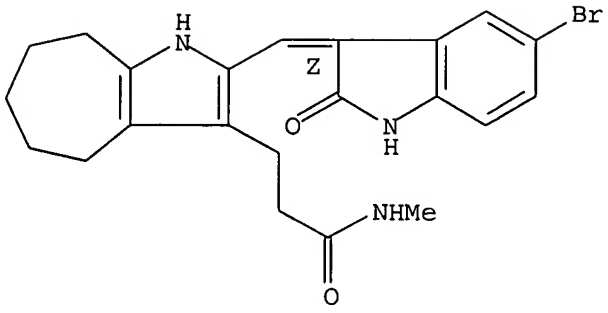
RN 760998-07-0 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



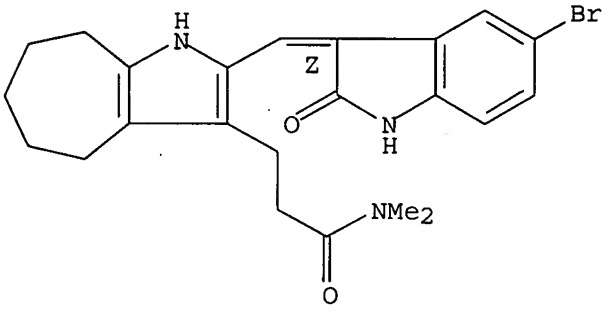
RN 760998-08-1 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro-N-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



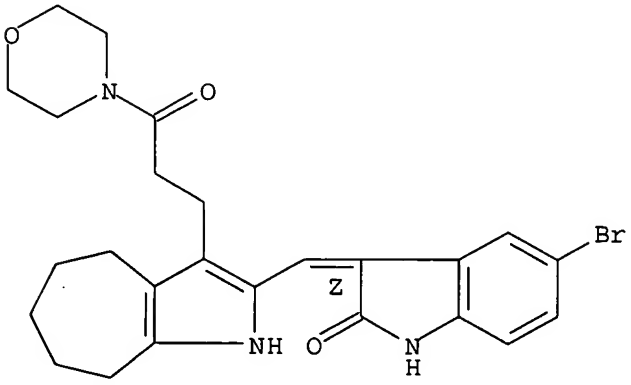
RN 760998-09-2 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 760998-10-5 HCAPLUS
CN Morpholine, 4-[3-[2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-3-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

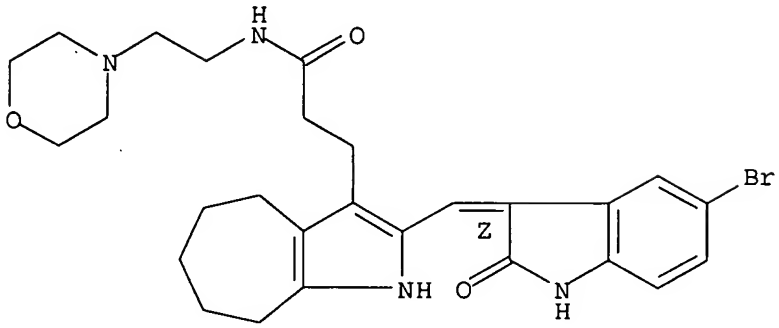
Double bond geometry as shown.



RN 760998-11-6 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro-N-[2-(4-morpholinyl)ethyl]-

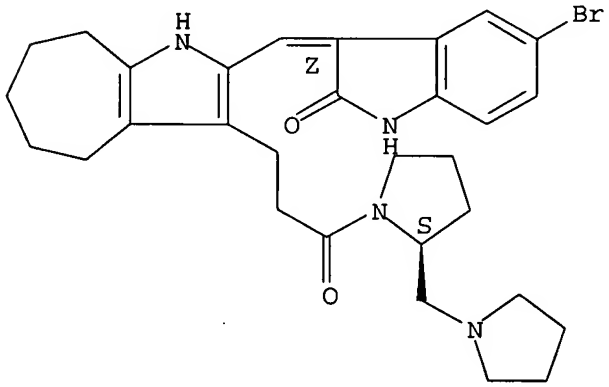
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



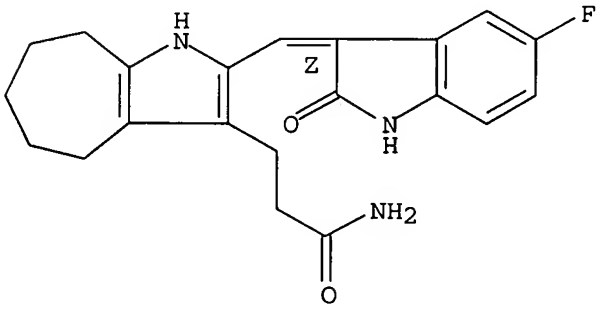
RN 760998-12-7 HCAPLUS
CN Pyrrolidine, 1-[3-[2-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-3-yl]-1-oxopropyl]-2-(1-pyrrolidinylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



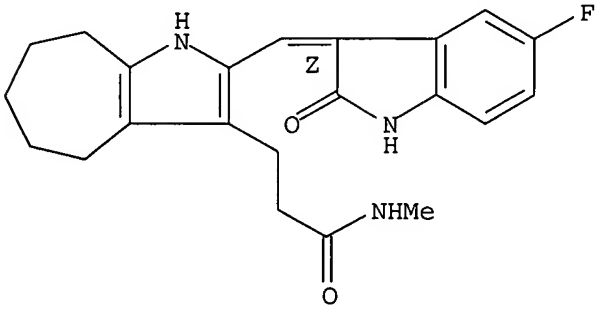
RN 760998-13-8 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



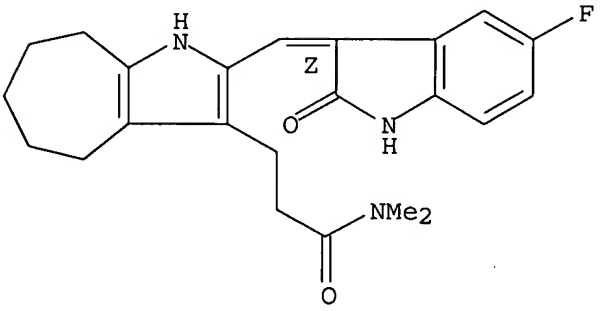
RN 760998-14-9 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro-N-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



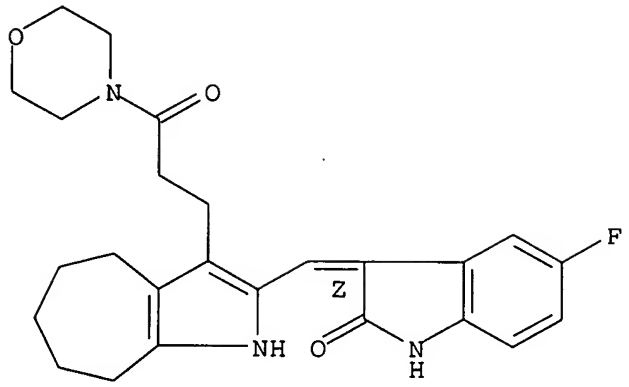
RN 760998-15-0 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



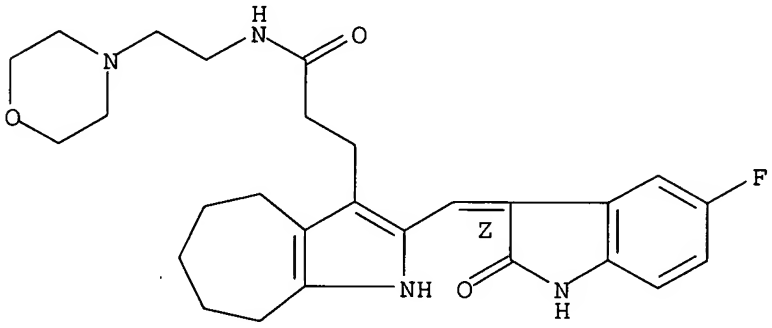
RN 760998-16-1 HCAPLUS
CN Morpholine, 4-[3-[2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-3-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



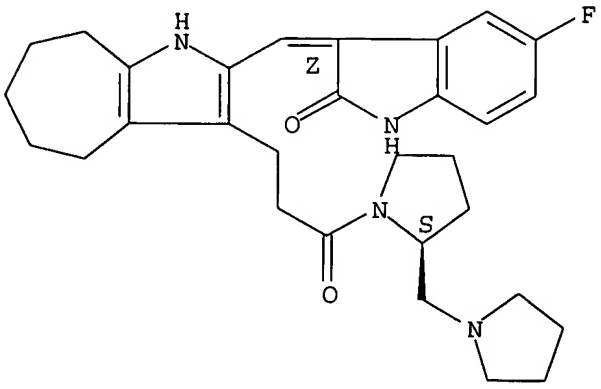
RN 760998-17-2 HCAPLUS
CN Cyclohepta[b]pyrrole-3-propanamide, 2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 760998-18-3 HCAPLUS
CN Pyrrolidine, 1-[3-[2-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrol-3-yl]-1-oxopropyl]-2-(1-pyrrolidinylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	124.62	467.18

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-30.00	-30.00

STN INTERNATIONAL LOGOFF AT 14:42:29 ON 07 MAR 2006